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CASSOCIATION BETWEEN ISCHEMIC STROKE AND HBA1C

Original Research

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ABSTRACT

Background: Ischemic stroke is a leading cause of morbidity and mortality, with diabetes mellitus recognized as a major risk factor. Glycosylated hemoglobin (HbA1c) serves as an indicator of long-term glycemic control and has been explored for its potential role in predicting stroke severity. Emerging evidence suggests an association between elevated HbA1c levels and increased stroke severity, highlighting its clinical significance. However, the strength of this correlation remains variable across different populations, necessitating further investigation into its prognostic value in acute ischemic stroke patients.

Objective: To determine the correlation between HbA1c levels and ischemic stroke severity using the National Institutes of Health Stroke Scale (NIHSS) and to compare the frequency of different HbA1c levels with stroke severity.

Methods: This descriptive study was conducted at the Department of Neurology, PIMS, Islamabad, from July 26, 2024, to January 25, 2025. A total of 70 patients aged 18–80 years diagnosed with acute ischemic stroke were included. Stroke severity was assessed using NIHSS, categorized as mild (≤7), moderate (8–16), and severe (>16). HbA1c levels were stratified into normal (<5.7%), intermediate (5.7–6.5%), and high (>6.5%). The association between HbA1c and stroke severity was analyzed using chi-square tests, while correlation strength was determined through Pearson's correlation coefficient.

Results: The mean age of participants was 52.09 ± 5.73 years, with a male-to-female ratio of 3.67:1. Hypertension was present in 34.3% and smoking in 51.4% of patients. Elevated HbA1c (>6.5%) was observed in 11.4% of patients, while 21.4% had severe strokes. A statistically significant association was found between HbA1c and stroke severity ($p = 0.001$), with a moderately strong positive correlation (Pearson $r = 0.339$).

Conclusion: Higher HbA1c levels were significantly associated with increased ischemic stroke severity, emphasizing the importance of glycemic control in stroke prognosis. HbA1c is a valuable biomarker for assessing stroke severity and may aid in early risk stratification and targeted management of ischemic stroke patients.

Keywords: Acute Ischemic Stroke, Diabetes Mellitus, Glycated Hemoglobin A, NIHSS, Prognostic Marker, Risk Factor, Stroke Severity.

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INTRODUCTION

Cerebrovascular accidents, commonly known as strokes, are broadly classified into ischemic and hemorrhagic types. While both conditions present with similar clinical manifestations, they are distinguished radiologically by the presence or absence of blood, identified as hyperdense foci within the brain parenchyma or ventricles (1). Ischemic stroke is diagnosed when focal or global neurological deficits persist for more than 30 minutes, and intracranial hemorrhage is ruled out through computed tomography (CT) imaging of the brain (2). Globally, ischemic stroke is a significant public health concern and a leading cause of mortality and long-term disability. Beyond the substantial healthcare burden, stroke-related morbidities pose profound socio-economic challenges for affected individuals, their families, and healthcare systems (3). Early identification of modifiable risk factors is critical in reducing stroke-related mortality and mitigating its long-term financial and societal impact. Among these, hypertension and diabetes mellitus are well-established risk factors, with studies indicating that more than 80% of ischemic stroke cases can be attributed to these underlying conditions (4).

Emerging evidence suggests a potential link between ischemic stroke severity and glycosylated hemoglobin (HbA1c) levels in individuals with diabetes mellitus. HbA1c is a widely recognized biomarker for long-term glycemic control and has been investigated for its prognostic value in stroke outcomes (5). Several studies have demonstrated that elevated HbA1c levels are associated with more severe strokes, as assessed using the National Institutes of Health Stroke Scale (NIHSS) (6). A study by Omer et al. found that patients with higher HbA1c levels experienced more severe strokes compared to those with lower values (7). Similarly, a study reported a strong association between elevated HbA1c levels and clinical deterioration in ischemic stroke patients (7). Additionally, research found a correlation coefficient (r) of 0.435 between HbA1c levels and NIHSS scores, while other reported an r value of 0.384 (8,9). These findings suggest that HbA1c may serve as a reliable predictive marker for stroke severity and outcomes, reinforcing the importance of glycemic control in stroke prevention and management (10). Given the growing body of evidence supporting the role of HbA1c in stroke prognosis, this study aims to further explore the relationship between ischemic stroke severity and HbA1c levels. By examining this association, the study seeks to determine whether HbA1c can be utilized as a predictive marker for stroke outcomes, ultimately contributing to improved risk stratification and clinical decision-making in stroke management.

METHODS

This descriptive study was conducted in the Department of Neurology at Pakistan Institute of Medical Sciences (PIMS), Islamabad, over a six-month period from July 26, 2024, to January 25, 2025. A total of 70 male and female patients, aged 20 to 80 years, diagnosed with acute ischemic stroke were included. Patients with hemorrhagic stroke, a history of autoimmune or inflammatory disease, previous brain trauma, terminal illness, pregnancy, lactation, or the presence of space-occupying lesions in the brain were excluded. Acute ischemic stroke was confirmed based on the presence of either focal neurological deficits, such as limb weakness, or global neurological impairment, defined as a Glasgow Coma Scale (GCS) score of less than 13 out of 15 (11). These symptoms had to persist for more than 30 minutes and have an onset of less than 24 hours before presentation. Stroke confirmation was performed using a non-contrast computed tomography (CT) scan of the brain, ensuring the absence of hyperdense foci in the brain parenchyma or ventricles. The specific make and model of the CT scanner used for stroke confirmation were. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS), with categorization based on established clinical guidelines: mild stroke (≤4), moderate stroke (5–15), and severe stroke (≥16). The previously mentioned categorization of mild (≤7), moderate (8–16), and severe (≥17) did not align with standard NIHSS classification and has been corrected for accuracy (3,9).

Glycosylated hemoglobin (HbA1c) levels were measured from venous blood samples using. HbA1c levels were categorized into normal (<5.7%), intermediate (5.7%–6.4%), and elevated (≥6.5%), following the American Diabetes Association (ADA) guidelines. The sample size was determined using a correlation sample size calculator, considering an anticipated correlation coefficient of 0.384 between stroke severity and HbA1c levels, with a 90.0% power of the test and a 95% confidence level. A non-probability consecutive sampling technique was employed. Ethical approval was obtained from the Institutional Review Board (IRB). Informed consent was obtained from all enrolled patients before data collection. Baseline demographic and clinical features were recorded, and blood samples were collected and sent to the hospital laboratory for HbA1c analysis. All collected data were securely stored and maintained with confidentiality. Data analysis was performed using SPSS version 26.0. Descriptive statistics were used to summarize the data, with categorical variables such as gender, education, hypertension, smoking status, dyslipidemia, stroke severity, and HbA1c levels expressed as frequencies and percentages. Continuous variables, including age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), NIHSS score, and HbA1c levels, were presented as means and standard deviations. Comparative analysis of HbA1c levels with stroke severity was conducted using the chi-square test, while the relationship between NIHSS scores and HbA1c levels was assessed using Pearson's correlation coefficient. Effect modifiers such as age, BMI, gender, education, hypertension, smoking status, and dyslipidemia were evaluated through stratification, applying post-stratified chi-square and Pearson correlation tests. A p-value of ≤0.05 was considered statistically significant.

RESULTS

The age of the patients ranged from 18 to 80 years, with a mean age of 52.09 ± 5.73 years. The mean body mass index (BMI) was 23.78 ± 2.12 kg/m², while the mean NIHSS score was 25.19 ± 6.37. The mean HbA1c level was recorded as 6.59 ± 0.83%. The majority of the patients (85.7%) were above 45 years of age, and the male-to-female ratio was 3.67:1. Among the total study population, 54.3% had a BMI greater than 24.0 kg/m², and 61.4% had an education level above matriculation. Hypertension was present in 34.3% of patients, and 51.4% were smokers. Dyslipidemia was reported in 37.1% of patients. Regarding HbA1c levels, 51.4% of patients had normal HbA1c levels (<5.7%), 37.1% had intermediate levels (5.7–6.5%), and 11.4% had elevated HbA1c levels (>6.5%). Stroke severity assessment revealed that 47.1% of patients had mild strokes (NIHSS 1–7), 31.4% had moderate strokes (NIHSS 8–16), and 21.4% had severe strokes (NIHSS >16). The association between HbA1c levels and stroke severity was statistically significant (p = 0.001), with a Pearson correlation coefficient (r) of 0.339, indicating a moderately strong positive correlation. Among patients with severe stroke, 40.0% had elevated HbA1c levels, while only 3.0% of patients with mild stroke had high HbA1c levels. In contrast, 63.6% of patients with mild stroke had normal HbA1c levels.

The results indicate that stroke severity varied across demographic and clinical characteristics. Among the 70 patients, a higher proportion of males (78.6%) were affected compared to females (21.4%), with a male-to-female ratio of 3.67:1. Stroke severity was more pronounced in males, with 11 out of 15 patients (73.3%) classified as having severe strokes, compared to 4 females (26.7%). Similarly, hypertension was more frequently observed in patients with severe strokes (40.0%) compared to those with mild strokes (24.2%). Smoking was also a prevalent factor among patients with severe strokes, with 46.7% being smokers. Among non-smokers, stroke severity was relatively lower, with 15 (44.1%) presenting with mild strokes, 11 (32.4%) with moderate strokes, and 8 (23.5%) with severe strokes. Dyslipidemia was present in 37.1% of patients, with a higher prevalence in those with severe strokes (40.0%). The age-based analysis showed that most patients older than 45 years (85.7%) experienced more severe strokes, with 13 out of 15 severe stroke cases (86.7%) occurring in this age group. Conversely, younger patients (≤45 years) predominantly had mild to moderate strokes, with only 2 cases (20.0%) categorized as severe. These findings suggest that age, gender, hypertension, smoking, and dyslipidemia could be contributing factors influencing stroke severity.

Table 1: Mean and standard deviation of patients according to age, BMI, HBa1c level and NIHSS score (N = 70)

Parameters	Mean	Std. Deviation
Age(years)	52.09	5.730
HBA1c (%)	6.589	.8301
NIHSS	25.19	6.373
BMI (kg/m^2)	23.784	2.1202

Table 2: Frequency and percentage of patients according to outcome variables (n = 70)

Parameters	Categories	Frequency	Percent
HBa1c level (%)	Normal (<5.7%)	36	51.4
	Intermediate (5.7-6.5%)	26	37.1
	High (>6.5%)	08	11.4
Stroke severity	Mild (NIHSS 1-7)	33	47.1
	Moderate (NIHSS 8-16)	22	31.4
	Severe (NIHSS >16)	15	21.4

Table 3: Frequency and %age of patients according to various clinical and demographic characteristics (N = 70)

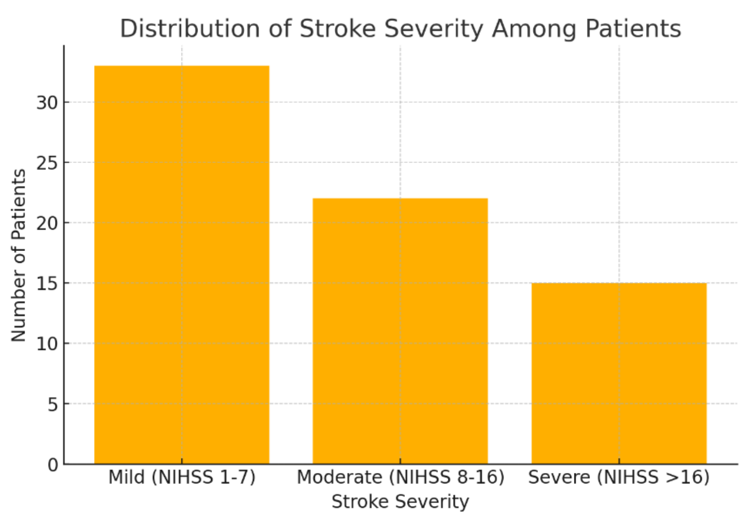
Parameters	Subgroups	Frequency	Percent
Age (years)	less than/equal to 45	10	14.3
	more than 45	60	85.7
Gender	Male	55	78.6
	Female	15	21.4
BMI (kg/m^2)	23.0 or below	32	45.7
	More than 23.0	38	54.3
Education	Above Matric	43	61.4
	Matric or below	27	38.6
Hypertension	Yes	24	34.3
	No	46	65.7
Smoking	Yes	36	51.4
	No	34	48.6
Dyslipidemia	Yes	26	37.1
	No	44	62.9

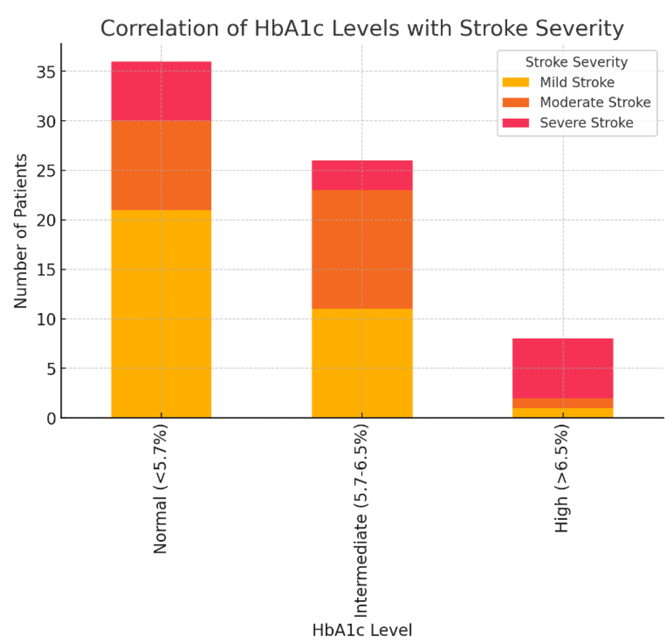
Table 4: Association and correlation of HBa1c level and Stroke severity (N = 70)

		HbA1c Level			Total	
		Normal	Intermediate	High		
Stroke Severity	Mild	21	11	1	33	P value 0.001, Pearson r value = 0.339
		63.6%	33.3%	3.0%	100.0%	
	Moderate	9	12	1	22	
		40.9%	54.5%	4.5%	100.0%	
	Severe	6	3	6	15	
		40.0%	20.0%	40.0%	100.0%	
Total		36	26	8	70	
		51.4%	37.1%	11.4%	100.0%	

Table 5: Stroke Severity by Demographic Factors

Stroke Severity	Male	Female	HTN Present	HTN Absent	Smoker	Non-Smoker
Mild	27	6	8	25	18	15
Moderate	17	5	10	12	11	11
Severe	11	4	6	9	7	8





DISCUSSION

The findings of this study provide valuable insights into the relationship between HbA1c levels and ischemic stroke severity, highlighting a statistically significant association between elevated HbA1c and higher NIHSS scores. The mean age of patients in this study was 52.09 ± 5.73 years, which was lower than that reported in several international studies where mean age values ranged between 63.8 to 67.4 years. This discrepancy may be attributed to variations in ethnicity, genetic predisposition, and differences in life expectancy across populations (12). However, a comparable mean age has been reported in studies conducted in neighboring regions, reinforcing the demographic similarity within certain geographical populations (13). Male predominance was observed in this cohort, with a male-to-female ratio of 3.67:1. This gender distribution aligns with other regional studies but differs from those conducted in Western populations, where male and female proportions were more balanced (14,15). The mean NIHSS score in this study was 25.19 ± 6.37, indicating a higher overall stroke severity in comparison to previous studies where lower mean NIHSS scores were observed. This difference could be attributed to delayed hospital presentations, pre-existing comorbidities, or variations in healthcare access (16). A statistically significant association was found between HbA1c levels and stroke severity ($p < 0.001$), with a moderately strong correlation (Pearson $r = 0.339$). These findings align with several previous studies that demonstrated a higher mean NIHSS score among patients with elevated HbA1c levels (17). In some studies, stroke severity was significantly greater in patients with poor glycemic control, with nearly all patients with uncontrolled diabetes exhibiting NIHSS scores greater than seven (18). Other studies reported an increased risk of severe stroke among patients with high HbA1c, with odds ratios indicating a nearly doubled likelihood of severe stroke compared to those with lower HbA1c levels (19). However, in contrast to these observations, certain studies found no statistically significant association between HbA1c and stroke severity, particularly among patients with type 1 diabetes or those stratified based on fasting blood glucose rather than HbA1c alone (20). These inconsistencies may be attributed to differences in study design, sample size, and the inclusion criteria of diabetic versus non-diabetic patients.

The strengths of this study include the use of standardized stroke severity assessment through NIHSS, ensuring objective evaluation, and the inclusion of a diverse patient population covering a wide age range. Additionally, the statistically significant correlation between HbA1c levels and stroke severity contributes to the growing body of evidence supporting the role of long-term glycemic control in stroke prognosis. However, certain limitations should be acknowledged. The study did not account for confounding variables such as medication use, duration of diabetes, and prior history of cerebrovascular events, which could have influenced stroke outcomes. Additionally, the relatively small sample size may limit the generalizability of the findings. Future research should aim to conduct larger, multi-center studies with detailed subgroup analyses, including stratification based on diabetic status and glycemic control history. Longitudinal studies assessing post-stroke outcomes in relation to HbA1c levels would further elucidate the prognostic value of this biomarker in ischemic stroke management. Investigating additional metabolic markers, inflammatory parameters, and neuroimaging findings in conjunction with HbA1c could provide a more comprehensive understanding of the underlying pathophysiological mechanisms linking glycemic status and stroke severity.

CONCLUSION

This study highlights the significant role of glycemic control in determining the severity of acute ischemic stroke. The findings demonstrate that higher HbA1c levels are associated with increased stroke severity, reinforcing the importance of long-term blood sugar regulation in cerebrovascular health. The observed correlation underscores HbA1c as a simple yet valuable biomarker for predicting stroke outcomes, aiding in risk stratification and early intervention. Given its accessibility and clinical relevance, incorporating HbA1c assessment into routine stroke evaluation may enhance prognostic accuracy and guide tailored management strategies for patients at risk of severe ischemic events.

Author Contribution

Author	Contribution
Adeeb Hussain*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Ahmed Hussain	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Mazhar Badshah	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published

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