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Research Article

# Association Between Hemoglobin A1C and the Severity of Acute Ischemic Stroke in Sudanese Patients in Omdurman Military Hospital

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## Abstract

**Background:** Hemoglobin A1C (HbA1c) levels are known to be linked to a higher risk of stroke. However, no research data is available on the impact of HbA1C on the severity of acute ischemic stroke in Sudan.

**Methods:** This study is a descriptive, cross-sectional hospital-based study of 40 cases of acute ischemic stroke. Ischemic stroke was confirmed using computed tomography (CT) scan at admission; all subjects' blood HbA1C levels were also measured. Participants were divided into two subgroups based on HbA1C at admission, **good glycemic control (GGC)** (<7 HbA1C) and **poor glycemic control (PGC)** (>7 HbA1C), and neurological impairment was assessed using the National Institutes of Health Stroke Scale (NIHSS).

**Results:** The age distribution of the participants was 45-85 years, with an average age of 63.5±9.2 years with the highest frequency (67.5%) in the age group of 55-75 years. PGC had a statistically significant high HbA1C value of 8.9±1.3 ($P$=0.000), when compared to GGC subgroups 5.1±0. The association between stroke severity and HbA1C levels on admission in this study was statistically significant ($P$ value=0.005), on admission (78.6%) PGC had moderate to severe stroke (> 18.8 NIHSS) versus (33.3%) that of the GGC (>10.4NIHSS). The frequency of elevated HbA1C levels in patients with acute ischemic stroke was 70% in this study.

**Conclusion**: PGC was shown to be linked to the occurrence of stroke and to its severity.

**Keywords:** ischemic stroke, HbA1C, NIHSS

## 1. Introduction

A total of 17 million people worldwide had a stroke in 2010. Between 1990 and 2010, the number of strokes in developed countries declined roughly by 10%, while it grew by 10% in developing countries [1]. Stroke is a major health problem in the Middle East, causing severe disability and death, with a fatality rate that is anticipated to double by 2030 [2].

According to the most recent World Health Organization (WHO) data, stroke fatalities in Sudan were 27,222, or 10.17% of all deaths, placing Sudan at number 27 in the world. Although the risk factors for stroke in Sudan are similar to those in developed nations, the peak age group for mortality in Sudan is a decade earlier than in the developed countries [3].

As in many other low- and middle-income nations, the prevalence of diabetes mellitus (DM) began to rise in Sudan. It is expected to affect 8% of the population but has reached 19% in some northern states [4, 5, 6]. Although it has been linked to inheritance in some cases, obesity is responsible for 40% of cases [7]. Because most patients cannot afford the medicine, PGC has resulted in chronic diabetes problems (treatment is not readily available and poor quality of life [8, 9, 10]. The Sudanese community's sedentary lifestyles and bad dietary habits make it difficult to implement preventive measures, but patients with diabetes require lifetime treatment, which is difficult to maintain in a state where insolvency is the norm [11].

NIHSS is a widely used clinical assessment tool to assess the severity of stroke patients, determine appropriate treatment, and predict patient outcomes. "The NIHSS is a 15- neurologic examination stroke scale item that evaluates the effect of acute cerebral infarction on the levels of consciousness, language, neglect, visual field impairment, extraocular movement, motor strength, ataxia, dysarthria, and sensory impairment level. Each item is assigned a score from 0 to 4, with 0 as normal, and there is an allowance for items that cannot be tested [12].

HbA1C levels have been linked to stroke in the past. However, no research has been done in Sudan on the impact of HbA1C on the severity of stroke in acute cases. In Sudan, strategies to prevent stroke and improve outcomes remain insensitive and ambiguous due to a lack of documented evidence and the impacts of their implementation. These strategies include increasing public awareness and understanding of stroke, preventing and managing recognized risk factors for stroke, and treating stroke patients in the stroke ward.

## 2. Materials and Methods

This was a descriptive hospital-based cross-sectional study from January 2019 to September 2020. It was held at one of the main military hospitals in Omdurman—a general hospital with a neurology section that caters primarily to military personnel and their families.

The sampling technique was total coverage of all patients with acute ischemic stroke presenting to Omdurman military hospital and who fulfilled the required criteria.

Among 69 patients admitted with stroke in the period between February and May, 16 were excluded due to hemorrhagic stroke, 7 patients had intravenous glucose before or during the study period, 3 patients had a chronic ischemic stroke (more than three months), 2 patients had a recent blood transfusion, and 1 had hemoglobinopathy (documented on history and medical records). The remaining 40 patients were included in the study. They were given information about the study in order to obtain their informed consent.

### 2.1. Data collection

Patient demographics, clinical results, laboratory, and radiographic findings were all covered in a questionnaire interview after patients assent. In the emergency room, each patient underwent a clinical evaluation that included blood pressure measurements and a neurological examination to determine the severity of their stroke using NIHSS. A venous blood sample was obtained and sent to the laboratory for HbA1C testing after an ischemic stroke was identified. (HbA1C levels in healthy adult males and females in Sudan range from 1.2% to 6.5%) [13].

Most current guidelines circulated by professional associations for diabetes, including the American Diabetes Association [14], recommend HbA1c <7% as the optimal target for glycemic control. As a result, the patients were divided into four groups:

1. Patients with good glycemic control (GGC): HbA1C **less than 7,**

2. Patients with poor glycemic control (PGC): HbA1C **greater than 7.**

3. Newly diagnosed diabetes: Random blood sugar (RBG) levels greater than 200 mg/dl/l, no history of diabetes, and HbA1C level **greater than 7.**

4. Stress hyperglycemic: RBG greater than 200 mg/dl /l, no history of diabetes, and HbA1C **less than 7%.**

Following the completion of the questionnaire, 5 mL of venous blood was obtained from each participant under sterile conditions. The blood was collected and deposited in ethylenediaminetetraacetic acid (EDTA) container for HbA1C testing (samples that were icteric, lipemic, hemolyzed, or bacterially contaminated were not used.), HbA1C was determined using a commercial reagent kit from Roche Company and a modified enzyme-linked immunosorbent assay (ELISA) reader known as COBAS Integra 800.

The study measured several dependent and independent variables, including the severity of ischemic stroke, HbA1C, demographic data, and other risk factors.

### 2.2. Data management and analysis

The accuracy of the data received at the end of each participant's contact was verified. All of the data was kept secure by utilizing a laptop with a password that only (the researcher) knew, as well as storing it in locked closets. Statistical Package for Social Science (SPSS) statistics version 16.0 was used for the statistical analysis. Absolute and relative frequencies were used to summarize categorical data (counts and percentages). The mean and 95% confidence interval, as well as the mean and standard deviation (SD) were used to portray quantitative data. For demographic and clinical data, parametric procedures (Chi-square test for categorical data, Student-t test for continuous data) were utilized because the data were normally distributed. Spearman's correlation coefficient was used to perform correlation analysis (r). Statistical significance was defined as a p-value of less than 0.05. Also, multiple linear regressions were used to determine the involvement of cofactors in acute ischemic stroke severity. Tables, graphs, and charts were used to examine the relationship between the dependent and independent variables.

## 3. Results

### 3.1. Demographic information

The study group's ages ranged from 45 to 85 years, with a mean age of 63.5±9.2 years, and with the highest frequency (67.5%) in the 55 to 75 age group. Males were 28 (mean age: 64.6±8.2 years) and females were 12 (mean age: 61±11.11years) with a male to female ratio of 2:1. A bulk of patients came from Khartoum, Algazira, Northern, and Kurdufan states, accounting for 30%, 22.5%, 10%, and 10%, respectively. However, 70% of the patients resided in their own homes, whereas 30% lived in retirement facilities, 77.5%

of the patients were married, 15% of those who took part have a university diploma, and 50% were unemployed.

All patients had a simple CT scan, with 75% of CT scans taking place within 24 hours of the onset of symptoms; one patient also had to undergo magnetic resonance imaging (MRI). In 47.5% of instances, an electrocardiogram (ECG) was conducted, and in 22.5% an echocardiogram (ECHO) was performed. In 10% of the patients, carotid ultrasonography and Doppler were performed. According to the Trial of Org 10172 in acute stroke treatment (TOAST) classification of stroke subtypes, 25% of cases were caused by cardiac embolism, while the remaining 75% were unknown.

## 3.2. Patient's risk factors

Hypertension (HTN) is the leading cause (47.5%) of risk factors for ischemic stroke (47.5%), and DM is the second most common cause with 35%. It was found that 30% of the male patients smoked cigarettes, while 7.5% drank alcohol. In this study, 25% of the participants had heart illnesses, including atrial fibrillation (A.FIB) and carotid stenosis in one case. A history of peptic ulcer was found in 20% of the cases. Three of the patients who took part in the study had chronic renal disease. A family history of stroke at ages less than 55 was observed in 15% of the cases. Three patients had a history of past strokes.

## 3.3. Patient's investigations

Total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL), and low-density lipoprotein (LDL) measurements were taken for 4,5,3,3 patients respectively; this small number of samples could be related to the high cost of the tests. As a result, we did not look at their role in stroke severity.

## 3.4. Regression

A multivariate linear regression model was used to predict the severity of a stroke. This was based on an eight-predictor system, (stroke severity=-0.722+ (0.527) DM +0.008 age +0.125 A.FIB + (-0.258-) HTN +0.988 HbA1C level+0.208 smoking +0.724 alcohol consumption +0.000 RBG on admission) with F test (3.16) =2.626 and p-value =0.025, the model proved statistically viable for predicting stroke severity. To predict the severity of a stroke, the combination of the eight predictors accounted for r=0.636. Although all eight predictors played an effect on stroke severity, only the HbA1C level (p=0.001) had a statistically significant impact of 0.988. Age, DM, A.FIB, HTN, smoking, alcohol, and RBG each contributed (0.008, 0.527, 0.125, -0.258-, 0.208, 0.724, 0.000) but were not significant (p=0.613, 0.720, 0.308, 0.492, 0.229, 0.712 respectively).

Table 1: The mean and standard deviation of age between participant genders.

| Gender | Number | Mean of age | Std. Deviation |
|---|---|---|---|
| Male | 28 | 64.6071 | 8.22525 |
| Female | 12 | 61.0833 | 11.17187 |
| Both | 40 | 63.5500 | 9.20410 |

Table 2: The characteristic and variation of categorical values in the study groups.

| No. | Variable | GGC (%) | PGG (%) | Total N (%) | Chi-square test | P-value |
|---|---|---|---|---|---|---|
| 1-Gender | Male | 9(75) | 19(67.8) | 28(70%) | 0.204 | 0.651 |
| | female | 3(25) | 9(32.2) | 12(30%) | | |
| 2-A.FIB | Yes | 5(41.6) | 5(17.9) | 10(25%) | 2.540 | 0.111 |
| | No | 7(58.4) | 23(82.1) | 30(75) | | |
| 3-HTN | Yes | 8(66.6) | 11(39.2) | 19(47.5) | 2.521 | 0.112 |
| | No | 4(33.4) | 17(60.8) | 21(52.5) | | |
| 4-DM | Yes | 3(25) | 11(39.3) | 14(35) | 0.754 | 0.385 |
| | No | 9(75) | 17(60.7) | 26(65) | | |
| 5-Smoking | Yes | 5(41.6) | 7(25) | 12(30) | 1.111 | 0.292 |
| | No | 7(58.4) | 21(75) | 28(70) | | |
| 6-Alcohol | Yes | 1(8.3) | 2(7.1) | 3(7.5) | .017 | 0.896 |
| | No | 11(91.7) | 26(92.9) | 37(92.5) | | |
| 7-TOAST | Cardio embolism | 5(41.7) | 5(17.8) | 10(25) | 2.540 | 0.111 |
| | Undetermined causes | 7(58.3) | 23(82.2) | 30(75) | | |

Table 3: The characteristic and variation of continuous values in the study groups.

| No. | GGC | PGC | Total | Levene test | P-value |
|---|---|---|---|---|---|
| 1-Age I | 65.3+/–11.6 | 62.8+/–8.1 | 63.5+/–9.2 | 0.053 | 0.430 |
| RBG on admission I | 167.25+/–79.5 | 220.50+/–127.4 | 202.75+/–115.3 | 0.050 | 0.196 |
| HbA1C | 5.1+/–0.5 | 8.9+/–1.3 | 7.75+/–2.05 | 0.003 | 0.000 |
| NIHSS | 10.4+/–5.0 | 18.8+/–4.6 | 16.3+/–6.1 | 0.392 | 0.000 |

## 4. Discussion

This study has shown that the peak age group for stroke is 10 years less than in industrialized nations, yet Sudan has the same stroke risk factors as other countries;

Table 4: The association between stroke severity and HbA1C categories on admission.

| No. | NIHSS | GGC N (%) | PGC N (%) | Total N (%) | Chi-square | P-value |
|---|---|---|---|---|---|---|
| 1- | Moderate stroke | 8 (66.7) | 6 (21.4) | 14 (35) | 10.48 | 0.005 |
| | Moderate to severe stroke | 4 (33.3) | 9 (32.1) | 13 (32.5) | | |
| l | Severe stroke | 0 (0) | 13 (46.5) | 13 (32.5) | | |

Table 5: The correlation between NIHSS and HbA1C.

| | | National Institutes of Health Stroke Scale | HbA1C categories |
|---|---|---|---|
| National Institutes of Health Stroke Scale | Pearson Correlation | 1 | 0.512** |
| | Sig. (2-tailed) | | 0.001 |
| | *N* | 40 | 40 |
| Category | Pearson Correlation | 0.512** | 1 |
| | Sig. (2-tailed) | 0.001 | |
| | *N* | 40 | 40 |
| **Correlation is significant at the 0.01 level (2-tailed). | | | |

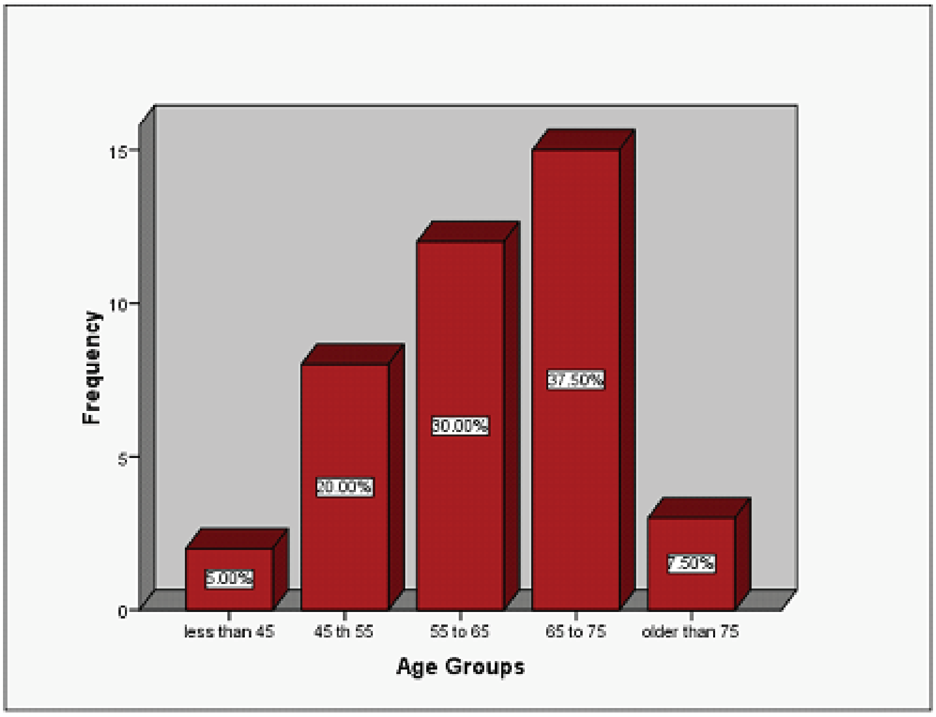


**Figure 1**: The percentage of age distribution among participant.

the most common is hypertension, which is followed by diabetes mellitus. However, the number of patients in this study is small and a bigger study is needed to determine the risk factors influencing this population.

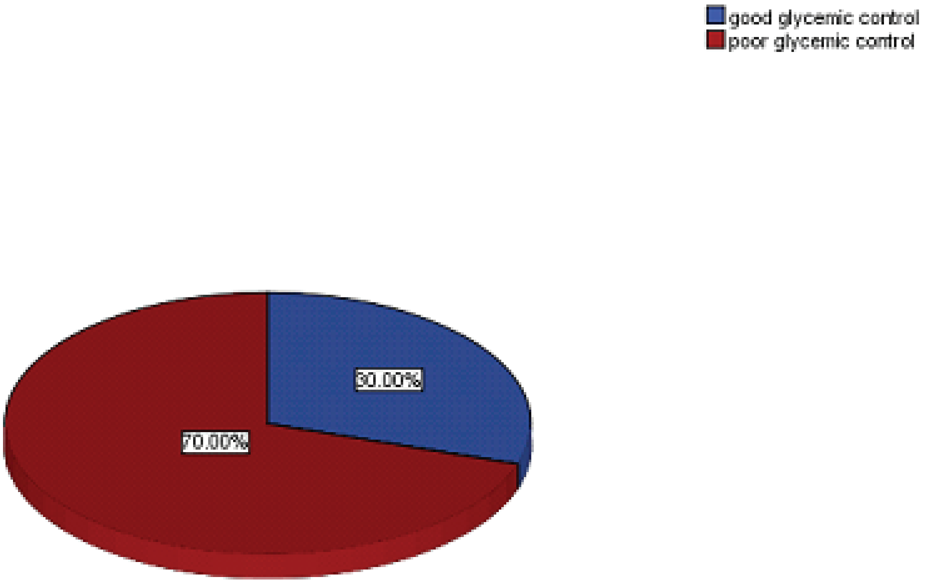


**Figure 2**: The glycemic status based on HbA1C.

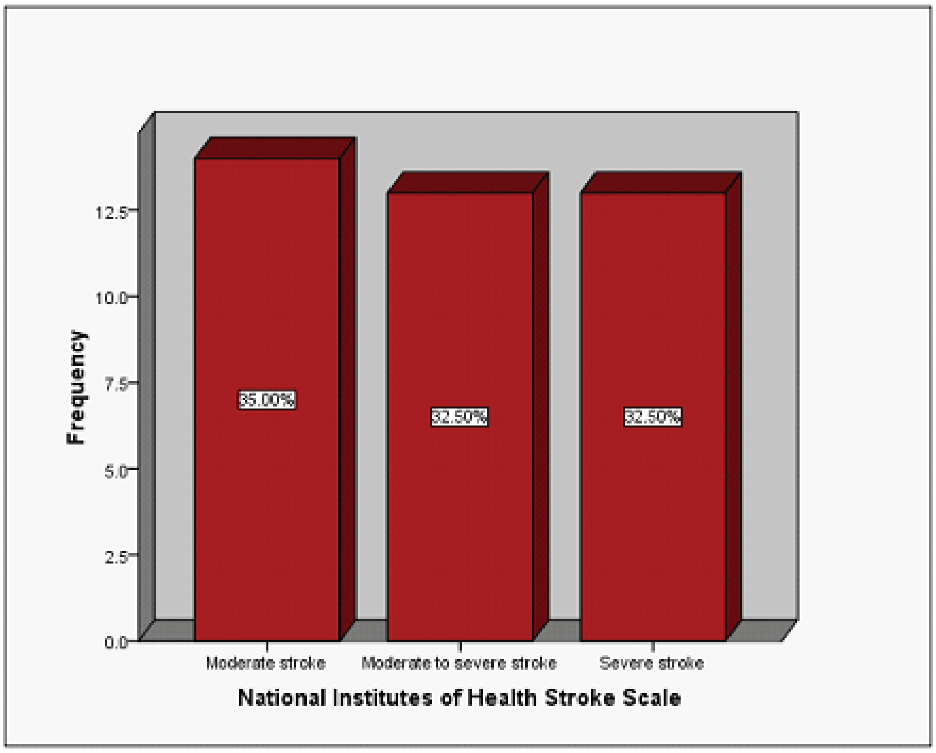


**Figure 3**: The stroke severity classification based on NIHSS.

The sex distribution was dominated by men and this conclusion is in line with the findings of other epidemiological studies [2, 15,16].

Only 36 individuals were subjected to an RBG test when they were admitted. Of those diagnosed with diabetes, 38.5% had hyperglycemia while 61.5% were euglycemic.

Hyperglycemia was seen in 34.8% of nondiabetic patients; however, 17 patients were diagnosed with DM at the time of admission. Perttu J. Lindsberg and Risto o Roine [17] found that two-thirds (66%) of all patients with ischemic stroke had hyperglycemia, whereas hyperglycemia was found in 36.1% of patients in our study. They also said that known diabetes and newly diagnosed diabetes patients made up to one-third of the cases (33%) and those same groups made up to 32.5 % of the study participants.

In comparison to the study by Naveed *et al.*, the PGC group constituted 24.7 %, while in this study PGC group comprised 70% of the study participants [18]. PGC had a statistically significant association with HbA1C value 8.9+/-1.3 (*P* value 0.000) when compared to GGC 5.1+/-0.5; another study found a similar result (8.510+/- 1.260) in PGC and (5.921 +/_0.501) in GGC [19]. On admission, PGC group had an RBG of 220.50+/-127.4 and GGC group had an RBG of 167.25+/-79.5. Men in PGC accounted for 67.8% of the participants, whereas women accounted for 32.2 %. In PGC, the average age was 62.8+/-8.1 while in GGC it was 65.3+/-11.6. People aged between 55 and 75 years accounted for 52.5% of all PGC, which could explain why the age of beginning of stroke in Sudan is 10 years earlier than in industrialized nations [3], despite the fact that this number is insignificant (*P* value=0.249). It is possible that this is due to the small number of participants.

On admission, 78.6% of PGC patients had a moderate to severe stroke (NIHSS > 18.8) compared to 33.3% of GGC patients (NIHSS > 10.4), which was statistically significant (p value=0.005), another study [19] found that (90%) of PGC patients had moderate to severe stroke (> 7NIHSS) at the time of admission, compared to (46.63%) of GGC patients.

HbA1C and stroke severity had a statistically significant relationship, with coefficients of determination (r 2=26.2) of r=0.512, p=0.001, assuming a non-normal distribution of either of the variables, Spearman Rank Correlation r=0.511, p=0.001, (r2=26.1), in both tests HbA1C levels and the severity of the stroke were statistically significant. This result was in line with findings from other investigations [19,20,21] with an R square of .512, the regression equation is NIHSS= (2.417+917*HbA1C) was statistically significant (F (1, 18) = 13.467, p=.001).

According to the findings of this study, higher HbA1C levels account for 70% of individuals with acute ischemic stroke. Stroke severity has been linked to PGC. HbA1C levels are a predictor of the degree of neurological impairment in individuals with acute ischemic stroke when measured on admission.

We recommend that based on the above-mentioned findings:

1- Patients who have had an ischemic stroke should be tested for hyperglycemia or an increased HbA1C level to avoid permanent hyperglycemia and other complications.

2- Due to the high-mortality rate from stroke conditions in Sudan, a well-equipped stroke clinic and epidemiologic research center are urgently needed to fulfill the following goals:

I. A program for prevention and control should be implemented and made feasible (especially at the level of primary health care, the general public should be aware of the symptoms of stroke, and the importance of early access to medical services).

II. Determine the prevalence and incidence of stroke.

III. Carry out more research to see if improved glycemic management before a stroke might improve the clinical course and outcome of those who have had an acute ischemic stroke.

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## Ethical Considerations

Ethical approval was obtained from Al-Neelain Institutional Review Board, Omdurman military hospital, and informed consent were obtained from all patients with confidential information. Patients were informed that they could refuse to take part in the study.

## Competing Interests

None declared.

## Availability of Data and Material

All data and materials associated with this paper were available through the corresponding author upon reasonable request.

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