OPEN ACCESS

Research Paper

Assessment of Serum HbA1c in Ischemic Stroke Patients

***Ahmed Dahham Al- Ali*[1], *Sajid I. Kadhim Alhussaini*[2]**

ABSTRACT:

BACKGROUND:

A stroke or cerebrovascular accident is defined as an abrupt onset of a neurologic deficit that is attributable to focal vascular cause. Hyperglycemia is a well-known predictor of poor outcomes in patients with acute ischemic stroke. Admission hyperglycemia has been associated with poor functional outcomes and increased mortality in patients with acute ischemic stroke.

OBJECTIVE:

To evaluate the HbA1C level in patient with ischemic stroke and its severity.

PATIENTS AND METHODS:

A cross-sectional study conducted at Baghdad teaching hospital, Baghdad, Iraq during a period from October 2020 to Feb 2021. The study included 50 patients who met the inclusion criteria, as well as, 50 individual (No stroke at time of data collection) as control group.

RESULTS:

The mean age of patients was 63.8 ± 10.2 years and males were represented 60% (30) of patients. The majority of patients were had hypertension (72%) and Diabetes Mellitus (56%). Among control group, only 8 patients were had hypertension while DM was presented in 29 (58%) patients. The mean HbA1C across patients was 8.02 ± 2.5, which was significantly higher in comparison to mean HbA1C across control group. The assessment of National Institutes of Health Stroke Scale score across patients showed that, a significant higher HbA1C among severs and moderate NHISS in comparison to mild NIHSS. Also, all mild NIHSS patients were in control status for HbA1C, while all severe NIHSS patients were uncontrolled. The distribution of HbA1C group was not equally across NIHSS. The multinomial logistic regress test showed, apart from HbA1C, which showed a strong association with NHSS, no association have been found between NHSS and other variables.

CONCLUSION:

A high HbA1C was associated with high NIHSS score in patients with stroke. There was a risk of 3.1 fold increase of stroke in patients with uncontrolled HbA1C.

KEY WORDS: Ischemic, stroke, HbA1c, Assessment, Patients.

[1]*Al-Yarmook Teaching Hospital, Baghdad, Iraq*
[2]*Retired, Baghdad Teaching Hospital, Baghdad, Iraq*

Iraqi Postgraduate Medical Journal, 2024; Vol. 23(2): 143-150
DOI: 10.52573/ipmj.2024.183543, Received: October 23, 2022, Accepted: October 15, 2023

INTRODUCTION:

A stroke or cerebrovascular accident is defined as an abrupt onset of a neurologic deficit that is attributable to focal vascular cause. The definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis Stroke is divided into 2 broad categories that define its pathophysiology, ischemic strokes and hemorrhagic strokes.(1)

Hyperglycemia is a well-known predictor of poor outcomes in patients with acute ischemic stroke. Admission hyperglycemia has been associated with poor functional outcomes and increased mortality in patients with acute ischemic stroke. This may be explained by the fact that hyperglycemia could be linked to exacerbation of ischemic brain injury, through free radical formation and enhancement of intracellular acidosis in ischemic penumbra. In addition, hyperglycemia can also cause neurovascular damage and blood-brain barrier disruption, which in turn lead to reperfusion injury after successful recanalization.(2)

Given these mechanisms, hyperglycemia can adversely affect prognosis in patients with acute ischemic stroke undergoing reperfusion therapy.

Although admission hyperglycemia may reflect preexisting abnormalities in glucose metabolism, however, it can also be the result of an acute stress reaction and inflammatory response after AIS, which could have a negative impact on prognosis. [3]

HbA1c (glycated hemoglobin) is a well-established marker for elevated glucose levels and is widely used to calculate the average glucose during the last 3 months in a patient to monitor diabetic vascular damage.[4] In this analysis, we investigated the predictive value of HbA1c levels to assess clinical outcomes in patients with acute ischemic stroke.

AIM OF THE STUDY:

To study the level of HbA1c in ischemic stroke and its severity.

PATIENTS AND METHOD:

This was a cross-sectional study to investigate the association and impact of HbA1C level on the occurrence of ischemic stroke and the severity of symptoms at time of admission, conducted at Baghdad teaching hospital, Baghdad, Iraq during a period from October 2020 to Feb 2021.

Inclusion and Exclusion Criteria

The study population involved all patients confirmed ischemic stroke clinically & imaging, *who met the following criteria:*

1) Subjects with clinically confirmed stroke in its acute phase (first 5 days).
2) Age between 18-85 years of both sexes, who gave informed consent to be included in this study.
3) Ischemic stroke.
4) Systolic BP > 90mmHg.

Exclusion criteria:

1) Insufficient or missing data.
2) Specific population: End stage kidney disease, dialysis, anemia, post thrombolysis & recent myocardial infarction.

Measuring the HbA1C

Blood has been drawn from each patient. The measurement of S.HbA1c level by COBAS INTEGRA 400 plus analyzer by using special reagent. Included patients whose HbA1C is < 7mg/dl consider controlled for DM, and uncontrolled group, whose HbA1C is ≥ 7mg/dl.

National Institutes of Health Stroke Scale: The NIHSS score have been used to assess the functional outcome for each patients based on NIHSS score.[5]

RESULTS:

The mean age of patients was 63.8 ± 10.2 years (range 42 – 85), while the mean age of control group was 45 ± 13 years (range 18 - 75). The males were represented 60% (30) of patients and females were represented 40% (20) of patients. The control group was matched in gender.

The majority of patients were had hypertension (72%) and DM (56%). Among control group, only 8 patients were had hypertension while DM was presented in 29 (58%) patients. There was significant higher number of patients with hypertension in comparison to control individuals (p value = 0.0001). While, the distribution of DM was equal across patients and control individuals (p value = 0.84). There were 8 patients were smokers, with 11 individuals among control group were smokers too, there was no significant difference in smoker distribution across both groups (p value = 0.44). Regarding the ischemic heart disease, there only 3 patients with history of IHD while no one among control group had IHD history. For pervious history of stroke and presence of atrial fibrillation, there were 4 and 5 patients had history of stroke and AF respectively, and there was a strong difference in presence of both history of stroke and AF among patients group in comparison to control group individuals (p value = 0.04 and 0.02 respectively). Table 1.

Table 1: Distribution of demographic characteristics across patients and control group.

Variable	Patients No. (%)	Control group No. (%)	P value*
Hypertension Yes No	 36 (81.8) 14 (25.0)	 8 (18.2) 42 (75.0)	0.0001
DM Yes No	 28 (49.1) 22 (51.2)	 29 (50.9) 21 (48.8)	0.84
Smoking Yes No	 8 (42.1) 42 (51.9)	 11 (57.9) 39 (48.1)	0.44
IHD Yes No	 3 (100) 47 (48.5)	 0 50 (51.8)	0.079
Previous Stroke Yes No	 4 (100) 46 (47.9)	 0 50 (52.1)	0.041
Atrial Yes No	 5 (100) 45 (47.4)	 0 50 (52.6)	0.022

**Chi-Square Test*

Glycated Hemoglobin

The mean HbA1C across patients was 8.02 ± 2.5, which was significantly higher in comparison to mean HbA1C across control group (p value = 0.004). Table 2.

Table 2. The HbA1C distribution across patients and control group.

HbA1C	Mean	SD	Range	P value*
Patients	8.02	2.5	5 – 14.7	0.004
Control	6.7	1.7	4.5 – 13.4	

*Independent Sample T test

The mean HbA1C across male patients was 7.7 ± 2.2 and across female patients was 8.4 ± 2.8, this difference did not reached the statistically significance (p value 0.29). Table 3.

Table 3: The HbA1C distribution across patients and control group.

HbA1C	Mean	SD	Std. Error	P value*
Male (30)	7.7	2.2	0.4	0.29
Female (20)	8.4	2.8	0.6	

**Independent Sample T test*

After HbA1C categorization (control < 7, and uncontrolled < 7), there were 26 (52.0%) patients had HbA1C more than 7, while among control group, there were 13 (26.0%) individual with HbA1C more than 7. This difference was significant (p value = 0.008) and there was a risk of 3.1 fold increase of stroke in patients with uncontrolled HbA1C (Odds ratio = 3.08, 95%CI = 1.3 – 7.1). Figure 1.

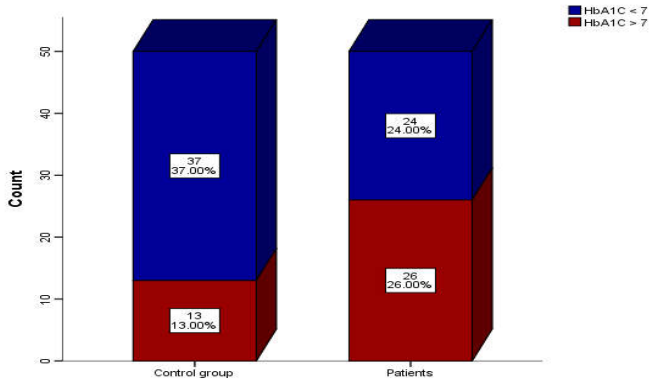

Figure 1: HbA1C distribution across participant.

To establish the confounders' contribution toward HbA1C among patients, a logistic regression test performed which show that, DM and previous stroke were associated with HbA1C. Table 4.

Table 4: Logistic regression test for HbA1C.

Variable	B factor	P value
Gender	-19.4	0.72
HT	1.3	0.65
DM	-73.3	0.001
Smoking	-52.3	0.9
IHD	-35.6	0.6
Previous Stroke	-19.7	0.045
AF	18.7	0.13

Stroke severity

The assessment of NIHSS score across patients showed that, a significant higher HbA1C among severs and moderate NHISS in comparison to mild NIHSS. Table 5.

Table 5: The HbA1C distribution across patients and control group.

NIHSS	N.	Mean	SD	St. Error	P value*
Mild	16	5.6	0.4	0.1	0.001
Moderate	25	8.2	1.9	0.39	
Sever	9	11.5	1.5	0.52	

**ANOVA test*

Also, all mild NIHSS patients were in control status for HbA1C, while all severe NIHSS patients were uncontrolled. The distribution of HbA1C group was not equally across NIHSS (p value = 0.001). Table 6.

Table 6:The distribution of HbA1C group across NIHSS.

NIHSS	HbA1C		Total	Chi-Squ	P value
	< 7 N. (%)	> 7 N. (%)			
Mild	16 (100)	0	16	28.2	0.001
Moderate	8 (32.0)	17 (68.0)	25		
Severe	0	9 (100)	9		

The multinomial logistic regress test has been performed to assess the association between the NHSS and study variables. Apart from HbA1C, which showed a strong association with NHSS, no association have been found between NHSS and other variables (p value > 0.05). Table 7.

Table 7: Multinomial logistic regression test for NHSS.

Effect	-2 Log likelihood of reduced model	Chi-Squ	P value
Gender	27.6	2.4	0.29
HT	29.7	4.5	0.1
DM	27.1	1.8	0.39
Smoking	28.1	2.9	0.23
IHD	27.1	1.8	0.41
Previous Stroke	25.3	0.1	0.9
AF	25.7	0.59	0.74

DISCUSSION:

Diabetes mellitus is an established risk factor for stroke. HbA1C is used to diagnose diabetes and to monitor the efficacy of treatment. Our aim is to evaluate the role of HbA1C as a simple routine test which can be done as a prediction of stroke risk factor and its higher level is associated with more severe symptoms.

The mean age of stroke patients in this study was comparable to other local study conducted by Basee's et al study in 2018, in which they found that the mean age of stroke patients was 63 years old.[6] Comparing to Asian countries, the mean age was relatively higher with stroke patients, in study from Korea, the authors found that the mean age was 66 years.[7] While the mean age was lower in comparison to European countries, which in Sweden the mean age was 73 years among patients with stroke.[8] This difference in the mean age of stoke patients might rely on different factors that included life style difference between our country and others, also the ethnicity, associated comorbidities, and stress could play an important role in developing of stroke in younger age group.[9]

It has been long understood that stroke incidence is higher in men than in women globally,[10] in this study, the males were representing 60% of patients which was in line with other studies that showed male predominance among patients with stroke.[2, 11, 12] Previously published data showed that the age is higher among males in comparison to females patients,[13] however, a more recent data suggested that stoke incidence is decreased among elderly males and overall now the incidence, in adjusted age between males and females, is equal.[14]

The majority of patients in this study were had hypertension which was comparable to other studies that showed more than 70% of their patients had hypertension at time of stroke.[2,3, 15] Hypertension continues to be the most prevalent modifiable risk factor for stroke globally, also hypertension is increased with age and it is more prevalent among elderly patients.[16, 17] There was significant higher number of patients with hypertension in comparison to control individuals which is in line with all previously mentioned studies.

Diabetes mellitus is a major risk factor for the development of stroke, particularly ischemic stroke, with type 2 diabetes mellitus alone known to increase stroke risk 1.5 to 4 fold. Microvascular complications of diabetes mellitus: ischemic heart disease (IHD), stroke, and peripheral vascular disease; represent a major cause of diabetes mellitus related mortality and health-related expenditure.[25] In this study, the DM was presented in more than half of the patients with stroke, this percentage was higher in comparable to Hjalmarsson's et al study, which showed a 25% of their patients were presented with DM.[3] Also, Lee's at al study, from Korea, they reported that around 35% of patients have DM at time of admission for stroke.[2] A study from Chine showed an even lower DM history in comparison to our study[7]. In Iraq, the prevalence of type 2 DM not studies very well, however, there are multiple studies conducted in specific areas of Iraq.

In Abbas study, the assessed the prevalence of DM in Basrah,[18] it showed that a very high prevalence (19.7%) of DM affecting one in five adults. Another studies conducted in north area of Iraq showed that the prevalence also high.[19] The higher prevalence of DM among Iraqi population may contributed to higher DM history among stroke patients in this study. The distribution of DM was equal across patients and control individuals who eliminated the bias of difference in DM prevalence between stroke patients and control individuals.

Ischemic heart diseases was presented in less than 7% of patients which was comparable to Chines study as it found that 7.9% of patients with stroke have a history of IHD.[7] Arterial fibrillation was presented in 10% of stroke patients which was higher than what observed in previously mentioned, in which it reported only 1.3% of their patients had AF, however, the main difference was the huge sample size included in Chines study.[7]

The smoking have a strong relationship with stroke and have been approved for decades,[20] however, in this study, the smoking status was comparable between the disease and control group.

The mean HbA1C across patients was 8.02 ± 2.5 which was higher in comparable to Lee's et al study, which found that the mean of HbA1C was 6 mg/dl.[2] The percentage of patients with HbA1C > 7 was presented in more than half of stroke patients in which it was relatively higher in comparison to Sweden study that showed only 13% of patients have HbA1C > 7.[3] Thus there was a risk of 3.1 fold increase of stroke in patients with uncontrolled HbA1C. Logistic regression test performed which show that, DM and previous stroke were associated with HbA1C. Which indicate that HbA1C have strong relationship with DM and previous stroke irrespective to other factors.

The assessment of NIHSS score across patients showed that, a significant higher HbA1C among severs and moderate NHISS in comparison to mild NIHSS, this strong association rise the negative impact of HbA1C among stroke patients. In Lee's et al study, they demonstrated no relationship between the initial NIHSS and HbA1C, however, they demonstrated that fasting blood sugar was strongly associated with initial NIHSS.[2] This discrepancy might rely on the fact that, in Iraq the patients with DM have poor glycemic control in comparison to other countries.[13] In Sweden, the assess beyond effect of HbA1C on functional outcomes only, and they including the death in which they found that the patients who presented with stroke and have HbA1C more than 6, have higher death rate and lower survival in comparison to stroke patients with HbA1C less than 6.[3] This demonstrated further the importance of HbA1C not only as predictor for poor functional outcomes, but also it could predict the survival of stoke patients.[21] Furthermore, Wang et al concluded from their study that "higher HbA1c on admission was an independent predictor of adverse functional outcome in ischemic stroke patients". Based on this point, tight glycemic control must be necessary for high-risk diabetic patients.[22] In Italy, also a study by Lattanzi's et al, they found that patients with high HbA1C have poorer outcome.[23] Also, the concluded that HbA1c values above the recommended goals increased the risk of unfavorable 3-month outcome.

The multinomial logistic regress test have been performed to assess the association between the NHSS and study variables showed that, the HbA1C is a single predictor factor for NIHSS score among stroke patients, in which to goes with Gao's et al study that demonstrated the strong association between the HbA1C and functional outcome.[24] Also, Kumar's et al study showed that HbA1C level at time of stroke patients admission might be a predictor for neurological impairment, severity, and functional outcomes.[25]

Having said that, the high HbA1C has been proved to be associated with unfavorable patient outcomes in terms of functional impairment and poorer outcomes in comparison to normal HbA1C levels in patients with stroke at the time of admission.

CONCLUSION:

HbA1C was associated with stroke prevalence among Iraqi patients with high HbA1C was associated with high NIHSS score in patients with stroke. There was a risk of 3.1 fold increase of stroke in patients with uncontrolled HbA1C

REFERENCES:

1. Khoshnam SE, Winlow W, Farzaneh M, Farbood Y, Moghaddam HF. Pathogenic mechanisms following ischemic stroke. Neurological Sciences. 2017;38:1167-86.
2. Lattanzi S, Bartolini M, Provinciali L, Silvestrini M. Glycosylated hemoglobin and functional outcome after acute ischemic stroke. Journal of Stroke and Cerebrovascular Diseases. 2016;25:1786-91.
3. Heo SH, Lee SH, Kim BJ, Kang BS, Yoon BW. Does glycated hemoglobin have clinical significance in ischemic stroke patients?.

Clinical neurology and neurosurgery. 2010;112:98-102.
4. Beck RW, Bergenstal RM, Cheng P, Kollman C, Carlson AL, Johnson ML, Rodbard D. The relationships between time in range, hyperglycemia metrics, and HbA1c. Journal of diabetes science and technology. 2019;13:614-26.
5. Lyden P. Using the national institutes of health stroke scale: a cautionary tale. Stroke. 2017 ;48:513-19.
6. Haitham H. Basee, Imad A. Lateef, Wissam F. Hassan. Review of stroke in Diyala-Iraq. International Journal of Advanced Research in Biological Sciences. 2018;5: 15-19.
7. Lee KJ, Lee JS, Jung KH. Interactive effect of acute and chronic glycemic indexes for severity in acute ischemic stroke patients. BMC neurology. 2018;18:1-7.
8. Hjalmarsson C, Manhem K, Bokemark L, Andersson B. The role of prestroke glycemic control on severity and outcome of acute ischemic stroke. Stroke research and treatment. 2014;2014, 6.
9. Shao IY, Elkind MS, Boehme AK. Risk factors for stroke in patients with sepsis and bloodstream infections. Stroke. 2019;50:1046-51.
10. Bushnell CD, Chaturvedi S, Gage KR, Herson PS, Hurn PD, Jiménez MC, Kittner SJ, Madsen TE, McCullough LD, McDermott M, Reeves MJ. Sex differences in stroke: challenges and opportunities. Journal of Cerebral Blood Flow & Metabolism. 2018;38:2179-91.
11. Benjamin, EJ, Blaha, MJ, Chiuve, SE Heart Disease and Stroke Statistics – 2017 update: a report from the American Heart Association. Circulation 2017;135:e146–e603.
12. 1 Liu H, Meng X, Liu CF, Wang D, Zheng H, Li H, Liu L, Wang Y, Wang Y, Pan Y. Higher hemoglobin A1c level is associated with poor outcome of intracerebral hemorrhage. Frontiers in neurology. 2019;10:1073.
13. Koton, S, Schneider, AL, Rosamond, WD Stroke incidence and mortality trends in US communities, 1987–2011. JAMA 2014;312:259–68.
14. Madsen, TE, Khoury, J, Alwell, K Sex-specific stroke incidence over time in the Greater Cincinnati/Northern Kentucky Stroke Study. Neurology 2017;89:990–96.
15. Hu L, Huang X, Zhou W, You C, Liang Q, Zhou D, Li J, Li P, Wu Y, Wu Q, Wang Z. Associations between resting heart rate, hypertension, and stroke: A population□based cross□sectional study. The Journal of Clinical Hypertension. 2019;21:589-97.
16. Upoyo AS, Setyopranoto I, Pangastuti HS. The Modifiable Risk Factors of Uncontrolled Hypertension in Stroke: A Systematic Review and Meta-Analysis. Stroke Research and Treatment. 2021;2021:1.
17. World Health Organization. The top 10 causes of death [homepage on the Internet]. Geneva: World Health Organization; 2017 [update 2017 January 12; cited 2018 July 12]. Available from: http://www.who.int/mediacentre/factsheets/fs310/en/.
18. Mansour AA, Al-Maliky AA, Kasem B, Jabar A, Mosbeh KA. Prevalence of diagnosed and undiagnosed diabetes mellitus in adults aged 19 years and older in Basrah, Iraq. Diabetes Metab Syndr Obes. 2014;7:139-44.
19. Alhabbo DJ, Saeed ID, Khalaf YA. Frequency of Type 2 Diabetes in Young Age Groups in Northern Iraq. Iraqi Journal of Medical Sciences. 2018;16.
20. Parikh NS, Chatterjee A, Díaz I, Merkler AE, Murthy SB, Iadecola C, Navi BB, Kamel H. Trends in Active Cigarette Smoking Among Stroke Survivors in the United States, 1999 to 2018. Stroke. 2020 ;51:1656-61.
21. Lau LH, Lew J, Borschmann K, Thijs V, Ekinci EI. Prevalence of diabetes and its effects on stroke outcomes: A meta□analysis and literature review. Journal of diabetes investigation. 2019 ;10:780-92.
22. Wang H, Chen S, Li X, Zhu Z, Zhang W. Impact of elevated hemoglobin A1c levels on functional outcome in patients with acute ischemic stroke. Journal of Stroke and Cerebrovascular Diseases. 2019 ;28:470-76.
23. Lattanzi S, Bartolini M, Provinciali L, Silvestrini M. Glycosylated hemoglobin and functional outcome after acute ischemic stroke. Journal of Stroke and Cerebrovascular Diseases. 2016;25:1786-91.
24. Gao Y, Jiang L, Wang H, Yu C, Wang W, Liu S, Gao C, Tong X, Wang J, Jin Y, Wu J. Association between elevated hemoglobin A1c levels and the outcomes of patients with small-artery occlusion: a hospital-based study. PLoS One. 2016;11:e0160223.

25. Kumar NS, Reddy A, Vallampalli G, Prasad PN. Role of HbA1c at admission on severity and functional outcome of ischemic stroke in patients with diabetes mellitus. Journal of Neurology & Neurophysiology. 2016;7:1-7.