



ORIGINAL RESEARCH PAPER

Geriatrics

CORRELATION OF GLYCATED HEMOGLOBIN AND STROKE RISK IN ELDERLY PATIENTS WITH OR WITHOUT DIABETES ATTENDING TERTIARY GERIATRIC CARE CENTRE

KEY WORDS: Hyperglycemia, Stroke, HbA1c

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ABSTRACT

Background : Diabetes poses a major health problem globally and is one of the top five leading causes of death in most developed countries. Diabetes potentiates stroke by favouring atherogenesis and thrombosis. It also increases platelet adhesiveness and decreases fibrinolytic capacity. Hyperglycemia predicts higher mortality and morbidity after acute stroke independently. **Aims and Objectives :** To comparatively evaluate stroke in diabetic and non diabetic Geriatric patients, to study the effect of glycemic levels on the outcome of stroke and to study the correlation between stroke and HbA1c level. **Material and Methods :** The study was carried out in Department of Geriatric Medicine, DY Patil University School of Medicine, a tertiary care hospital in Navi Mumbai on 30 diabetic and 30 non diabetic Geriatric patients admitted with history of acute stroke, confirmed by thorough physical examination and CT BRAIN, and those who satisfy inclusion and exclusion criterias were selected. **Results :** Percentage of male population in both the groups were higher. Previous history of stroke was present in 37% of diabetics and 13% of non-diabetic stroke patients. Diabetic patients had greater percentage of ischemic stroke (63%) as compared to non-diabetic patients (33%). Hemorrhages were less in diabetic stroke patients (37%) as compared to non-diabetics (67%). **Conclusion :** Diabetes is an independent risk factor for stroke. Stroke in diabetes differs from that of stroke in non-diabetics with respect to age, sex, stroke type, stroke severity, prevalence of risk factors and outcome.

INTRODUCTION

Glycated hemoglobin (HbA1c) has emerged as a useful biochemical marker reflecting the average glycemic control over the last 3 months, and the values are not affected by short-term transient changes in blood glucose levels¹

According to American Diabetes Association (ADA), nondiabetes usually falls within the 4.0%–5.6% HbA1c range. The prediabetes usually has the HbA1c levels as 5.7%–6.4%, while those with 6.4% or higher HbA1c levels have diabetes.^{2,3} As HbA1c functions as an indicator for the mean blood glucose level, it is now considered as an independent risk factor in diabetic patients⁴.

Since diabetes is associated with several comorbidities, the recommendations for individuals with diabetes include a healthy lifestyle (diet and exercise) and maintaining the HbA1c levels below 7.0%. Diabetes-related complications are directly proportional to the levels of HbA1c – the increase in the HbA1c levels also increases the risk of such complications.

Type 2 diabetes mellitus (T2DM), diagnosed as glycated hemoglobin (HbA1c) >6.5%, is a metabolic disorder characterized by insulin resistance that progresses to hyperglycemia⁵. It indicates long-term uncontrolled hyperglycemia in the body, which in diabetic patients leads to various vascular complications as a part of generalized atherosclerosis culminating ultimately into ischemic stroke⁶

An elevated level of HbA1c is now considered as an independent risk factor for cardiovascular disease in any subject with or without diabetes. For each 1% increase in HbA1c level increases the risk of CVD by 18% and positive association between HbA1c and CVD has been demonstrated in non-diabetic patients even within normal range of HbA1c⁷.

World Health Organisation defines the clinical syndrome of “stroke” as ‘rapidly developing clinical signs of focal (or global) disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin⁸

Although still widely used, the World Health Organization definition relies heavily on clinical symptoms and is now considered outdated by the American Heart Association and American Stroke Association due to significant advances in the nature, timing, clinical recognition of stroke and its mimics, and imaging findings that require an updated definition⁹.

Strokes represent a heterogeneous group of vascular pathologies that collectively act as a major global burden of mortality and lifelong morbidity. 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 fold¹⁰.

Patients with Diabetes mellitus (DM) are more prone to develop vascular diseases, including strokes. The increasing prevalence of diabetes makes it one of the most serious health problems in the world and its role in macrovascular complications such as stroke is of increasing importance¹¹.

Macrovascular 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^{12,13}

There are many factors which alter the outcome of stroke. Hyperglycemia predicts higher mortality and morbidity after acute stroke independently of other adverse prognostic factors, such as older age, type and severity of stroke and non-reversibility of the neurological deficit. The effect of hyperglycemia on mortality is large^{14,15,16}

Higher glycated hemoglobin levels were associated with an increased risk of first-ever ischemic stroke in both non-diabetes mellitus and diabetes mellitus cohorts. In people with established diabetes mellitus, higher glycated hemoglobin levels were associated with an increased risk of first-ever stroke.

Aims and Objectives

To comparatively evaluate stroke in diabetic and non

diabetic Geriatric patients, to study the effect of glycemic levels on the outcome of stroke and to study the correlation between stroke and HbA1c level.

MATERIAL AND METHODS

The study was carried out in Department of Geriatric Medicine, DY Patil University School of Medicine & Hospital, a tertiary care hospital in Navi Mumbai on 30 diabetic and 30 non diabetic Geriatric patients admitted with history of acute stroke, confirmed by thorough physical examination and CT BRAIN, and those who satisfy inclusion and exclusion criterias were selected.

The study was divided into 2 groups

Group I (n=30): Diabetic subjects

Group II (n=30): Non-diabetic subjects

Inclusion Criteria

1. Patients of either sex of more than 65 years of age.
2. Diabetes confirmed on the basis of past history of diabetes, history of taking oral hypoglycemic drugs or insulin, previous medical records suggestive of diabetes or previous reports of blood sugar or HbA1C confirming the diagnosis of diabetes according to WHO criteria.
3. Non-diabetics admitted with high blood sugar levels undergo repeat blood sugar (48 hours after admission) and HbA1C estimation.

Exclusion Criteria

1. Patients receiving diabetogenic drugs.
2. All uncommon strokes caused by hypercoaguable disorders, venous sinous thrombosis, vasculitis etc.

Fasting (at least 8 hours) venous blood samples were collected from the selected patients. Then, serum was analyzed for fasting blood sugar, lipid profile panel- Total cholesterol, Triglyceride, HDL-cholesterol and LDL-cholesterol, and HbA1c.

After obtaining informed consent, detailed history, clinical examination, lab investigation reports were entered in the Proforma specially designed for this study.

RESULTS

Sex Distribution and Diabetes

Sex	Diabetic		Non diabetic		Total
	n=30	%	n=30	%	
Female	12	40	12	40	24
Male	18	60	18	60	36

Past history and Diabetes

Past History	Diabetic		Non diabetic		P value
	n=30	%	n=30	%	
Hypertension	21	70.00	10	33.33	0.004
Ischemic heart disease	8	26.67	2	6.67	0.038
Previous stroke	11	36.67	4	13.33	0.037
No significant past history	0	0	18	60.00	0.00

HbA1C Outcome and Mean

Outcome	Diabetic		Non diabetic		P value	Mean+SD
	n=30	%	n=30	%		
Fair recovery (n=44)	19	63.33	25	83.33	0.004	6.22+1.27
Poor recovery (n=10)	8	26.67	2	6.67	0.038	8.35+1.56
Death (n=6)	3	10.00	3	10.00	0.037	8.75+2.46
Mean+SD	8.11		5.54			

DISCUSSION

In the present study out of 30 Diabetic stroke patients 18 (60%) were males and 12 (40%) were females whereas in Non-Diabetics 18 (60%) were males and 12 (40%) were females while in the study of Singh AS et al. (2013)¹⁷ 56 (60.9%) were males and 36 (39.13%) were females. Percentage

of male population in both the groups were higher.

HbA1c level is a good diagnostic tool but is also helpful for prognosis and to monitor therapeutic effects of drugs in diabetes. Well controlled and steady blood glucose levels can help prevent cardiovascular complications in patients with diabetes mellitus³

Previous history of stroke was present in 11 (37%) of diabetics and 4 (13%) of non-diabetic stroke patients. Diabetic patients had greater percentage of ischemic stroke 8 (27%) as compared to non-diabetic patients 2 (7%). 21 (70%) of diabetic stroke patients had past history of hypertension compared to 10 (33%) in non diabetic group which was statistically significant. In the study of Nazish S et al (2018) there were 193 (79.1%) patients with diabetes¹⁸.

19 (63.3%) had fair recovery in diabetic group as compared to 25 (83.3%) in non-diabetic group. 8 (26.7%) had poor recovery in diabetic and 2 (6.7%) had poor recovery in non-diabetic group. Death was seen in 3 (10%) of patients in both the groups. Overall outcome was better in the non-diabetic stroke patients. In the study of Hjalmarsson C et al. (2014) poor glycaemic control estimated via baseline HbA1c prior to stroke is an independent risk factor for poor survival and higher baseline HbA1c was a significant biochemical marker for increased stroke severity and unfavourable long-term functional outcome.¹⁹ In the study of Khaw KT (2004)²⁰ it was found that 15% of the deaths occurred in persons with diabetes

CONCLUSION

Diabetes is an independent risk factor for stroke. Stroke in diabetes differs from that of stroke in non-diabetics with respect to age, sex, stroke type, stroke severity, prevalence of risk factors and outcome. Glycated hemoglobin is directly associated with stroke risk, and improves the predictive accuracy for stroke in diabetic patients. The risk of stroke increases particularly at glycated hemoglobin level over 6.9%.

REFERENCES

1. Bao Y and Gu D. Glycated Hemoglobin as a Marker for Predicting Outcomes of Patients With Stroke (Ischemic and Hemorrhagic): A Systematic Review and Meta-Analysis. *Front.Neurol.*,2021;12:642899.
2. American Diabetes Association (ADA). Standards of medical care in diabetes. *Diabetes Care.*2014;37:S14-80)
3. American Diabetes Association (ADA). Diagnosis and classification of diabetes mellitus. *Diabetes Care.*2011;34:S62-9.)
4. Chintamani Bodhe, Deepali Jankar, Tara Bhutada, Milind Patwardhan, and Varsha Patwardhan. HbA1c: Predictor of Dyslipidemia and Atherogenicity in Diabetes Mellitus. *IJBMS* 2012;2(1):25-7.
5. Arnett DK, Blumenthal RS, Albert MA, et al. ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019;74:e177-232.
6. Singh AS, Atam V, Chaudhary SC, Sawlani KK, Patel ML, Saraf S, et al. Relation of glycated hemoglobin with carotid atherosclerosis in ischemic stroke patients: An observational study in Indian population. *Ann Indian Acad Neurol* 2013;16:185-9.
7. Joslin's Diabetes Mellitus 14th Ed Lippincott Williams & Wilkins Chapter 33: General approach to the treatment of diabetes mellitus.
8. Aho K, Harmans P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. *Bull World Health Organ* 1980;58: 113-130
9. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44:2064-2089).
10. SIGN Methodology Checklist 3: Cohort studies. Scotland: Scottish Intercollegiate Guideline Network; 2012. Available from: http://www.sign.ac.uk/assets/checklist_for_cohort_studies.rtf.2017.
11. Mokdad AH, Ford ES, Bowman BA, Nelson DE, Engelgau MM, Vinicor F, et al. The continuing increase of diabetes in the US. *Diabetes Care* 2001;24:412.
12. Greenland S. Quantitative methods in the review of epidemiologic literature. *Epidemiologic Reviews.* 1987;9:1-30.
13. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, Golden SH. Meta-Analysis: Glycosylated Hemoglobin and Cardiovascular Disease in Diabetes Mellitus. *Ann Intern Med.*2004;141:421-431.
14. Bell DS: Stroke in the diabetic patient. *Diabetes Care* 1994;17:213-19.
15. Stamler J, Vaccaro O, Neaton JD, Wentworth D, for the MRFIT Research Group: Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993; 16:434-44.
16. Neaton JD, Wentworth DN, Cutler J, Stamler J, Kuller L, for the MRFIT

- Research Group: Risk factors for death from different types of stroke. *Ann Epidemiol* 1993; 3:493-99.
17. Singh AS, Atam V, Chaudhary SC, et al. Relation of glycated hemoglobin with carotid atherosclerosis in ischemic stroke patients: An observational study in Indian population. *Ann Indian Acad Neurol* 2013; 16:185-9).
 18. Nazish S, Zafar A, Shahid R et al. Relationship Between Glycated Haemoglobin and Carotid Atherosclerotic Disease Among Patients with Acute Ischaemic Stroke. *Sultan Qaboos University Med J*, 2018; 18(3) : e311-317.
 19. Hjalmarsson C, Manhem K, Bokemark L, et al. The role of prestroke glycemic control on severity and outcome of acute ischemic stroke. *Stroke Res Treat* 2014; 2014:694569.)
 20. Khaw KT, Wareham N, Bingham S, et al. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. *Ann Intern Med* 2004; 141:413-20.)