ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

Clinical study of association of type 2 diabetes with severity and functional outcome of acute ischemic stroke at a tertiary care hospital

Ravi Kattimani[1], Sunil Kumar[2], Renuka Kattimani[3], Priyanka S.H.[4]

[1]Assistant Professor, Department of General Medicine, Shri B.M. Patil Medical College and Research Centre, Vijayapur, India.
[2]Associate Professor, Department of General Surgery, ESIC Medical College, Kalaburagi
[3]Consultant Ophthalmologist, Anugraha Eye Hospital, Superspeciality Eye Care and Laser Centre, Kalaburagi, India.
4.Assistant Professor, Department of Anaesthesia, Al-Ameen Medical College and Hospital, Vijayapur, India.

Received Date: 28/01/2023 Acceptance Date: 03/04/2023

Abstract

Background: Diabetes is known to increase the risk of stroke and worsen the clinical outcome in stroke patients. However, the exact mechanism by which diabetes induces stroke is unclear till date. Present study was aimed to study association of type 2 diabetes with severity and functional outcome of acute ischemic stroke at a tertiary care hospital. **Material and Methods:** Present study was single-center, prospective, observational study, conducted in patients of age >30 years, either gender, admitted with acute ischemic stroke, based on clinical findings of sudden onset of clinical symptoms of stroke, presence of focal/global neurological deficits or presence of an acute infarct as confirmed by either CT or MRI brain. **Results:** In present study, among 138 cases satisfying study criteria, majority were from 46-60 years age group (44.93 %), followed by from 61-75 years age group (36.96 %) and mean age was 69.45 ± 12.91 years. Males (54.35 %) outnumbered females (45.65 %). Patients were further divided into those with diabetes (n=45) and non-diabetic patients (n=93). Body weight (overweight/obese), family history of cardiovascular disease and chronic heart failure were common in diabetic patients as compared to non-diabetic patients and difference was statistically significant. Laboratory parameters such as HDL, TG, FBS, HbA1c and Uric acid were deranged in diabetic patients as compared to non-diabetic patients and difference was statistically significant. On admission, National Institutes of Health Stroke Scale score at admission in diabetic patients (9.1 ± 7.8) was more as compared to non-diabetic patients (8.3 ± 7.2) and difference was statistically significant. Diabetic patients had more adverse outcome (53.33 % vs 20.43 %) and more in-hospital mortality (22.22 % vs 11.83 %) and difference was statistically significant. **Conclusion:** Type 2 diabetes does not appear to affect ischemic stroke severity but is associated with a worse functional outcome at discharge.

Keywords: In-hospital mortality, diabetes mellitus, ischemic stroke, functional outcome

Corresponding Author: Dr. Priyanka S.H., Assistant Professor, Department of Anaesthesia, Al-Ameen Medical College and Hospital, Vijayapur, India.
Email: priyankahamilpurkar@gmail.com

Introduction

Stroke was defined according to WHO criteria as rapidly developing symptoms and/or signs of focal and at times global loss of cerebral function with no apparent cause other than that of vascular disease. Acute ischemic stroke (AIS) contributes to 87% of cases, primary

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

intracerebral hemorrhage (ICH) for 10%, and subarachnoid hemorrhage (SAH) for the remaining 3%.[1,2] Stroke is associated with an increased long-term morbidity in terms of physical, behavioural, and cognitive defects.

The main risk factor for stroke is high blood pressure. Other risk factors include tobacco smoking, obesity, high blood cholesterol, diabetes mellitus, a previous TIA, and atrial fibrillation. Diabetes mellitus is a metabolic disease prevalent throughout the world and its burden has been increasing in developing and underdeveloped countries. Diabetes mellitus by virtue of its microvascular and macrovascular complications plays a major role in the genesis of stroke. The incidence of stroke is higher in diabetics as compared to non-diabetics.[3]

Diabetes is known to increase the risk of stroke and worsen the clinical outcome in stroke patients. However, the exact mechanism by which diabetes induces stroke is unclear till date.[4] Similarly, risk of diabetes and stroke were reported to increase with advancing age.[4,5] This increased risk of ischemic stroke is largely attributed to the clustering of individual risk factors rather than from the separate vascular risk factors. Present study was aimed to study association of type 2 diabetes with severity and functional outcome of acute ischemic stroke at a tertiary care hospital.

Material And Methods

Present study was single-center, prospective, observational study, conducted in the Department of General Medicine, at Shri B M Patil medical college and hospital, Vijaypur, Karnataka, India. Study duration was of 2 years (January 2021 to December 2022). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients of age >30 years, either gender, admitted with acute ischemic stroke, based on clinical findings of sudden onset of clinical symptoms of stroke, presence of focal/global neurological deficits or presence of an acute infarct as confirmed by either CT or MRI brain & patients willing to participate in present study.

Exclusion criteria

- Patients with type 1 diabetes mellitus
- Intra cerebral haemorrhage
- Space occupying lesions
- Sub arachnoid haemorrhage
- Cerebral venous thrombosis
- Transient ischemic attacks
- Patients with recurrent cerebrovascular events

Study was explained to patients in local language and written consent was taken for participation and study. At admission, demographic data (age, sex), history of Type 2 DM and other cardiovascular risk factors [hypertension, atrial fibrillation, smoking, alcohol consumption, family history of CVD, chronic kidney disease], history of concomitant CVD [coronary heart disease (CHD), previous stroke, congestive heart failure] and pharmacological treatment were recorded. T2DM was defined as self-reported T2DM or antidiabetic treatment. Anthropometric parameters (weight, height, waist and hip circumference, waist to hip ratio) and systolic and diastolic blood pressure were also measured. The severity of stroke was assessed at admission with the National Institutes of Health Stroke Scale (NIHSS) score.

Routine laboratory investigations were performed after overnight fasting on the first day after admission and included serum levels of glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), creatinine, uric acid and HbA1c.

All patients without atrial fibrillation were treated with aspirin; clopidogrel was given to patients intolerant to aspirin. Patients who were on aspirin prior to stroke were switched to clopidogrel and vice versa. Patients with atrial fibrillation were treated with low-molecular

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

weight heparin. All patients were given a statin. Antihypertensive agents were discontinued during the acute phase of stroke except beta-blockers. Most patients with T2DM were treated with insulin during the acute phase of stroke. No patient underwent thrombolysis.
The outcome was assessed with the modified Rankin Scale (mRS) score at discharge and with in-hospital mortality. Adverse outcome was defined as mRS score at discharge ≥ 2 or in-hospital death. The length of hospitalization was also recorded.
Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) were calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.05 was considered as statistically significant.

Results

In present study, among 138 cases satisfying study criteria, majority were from 46-60 years age group (44.93 %), followed by from 61-75 years age group (36.96 %) and mean age was 69.45 ± 12.91 years. Males (54.35 %) outnumbered females (45.65 %).

Table 1: General characteristics

	No. of patients (n=138)	**Percentage(%)**
Age groups (in years)		
30-45	21	15.22
46-60	62	44.93
61-75	51	36.96
76-90	4	2.9
Mean age (in years)	69.45 ± 12.91	
Gender		
Male	75	54.35
Female	63	45.65

Patients were further divided into those with diabetes (n=45) and non-diabetic patients (n=93). Body weight (overweight/obese), family history of cardiovascular disease and chronic heart failure were common in diabetic patients as compared to non-diabetic patients and difference was statistically significant. While other risk factors alcohol consumption, smoking (current/past), coronary heart disease, previous ischemic stroke, chronic kidney disease and hypertension were comparable and difference was not significant statistically.

Table 2: Risk factors

Risk factors	**Diabetic (n=45)**	**Nondiabetic (n=93)**	**P value**
Body weight			
• Overweight	21 (46.67 %)	32 (34.41 %)	<0.001
• Obese	13 (28.89 %)	17 (18.28 %)	<0.001
Alcohol consumption	16 (35.56 %)	31 (33.33 %)	0.82
Smoking			
• Current	8 (17.78 %)	16 (17.2 %)	0.69
• Past	11 (24.44 %)	25 (26.88 %)	0.71
Family history of cardiovascular disease	14 (31.11 %)	21 (22.58 %)	<0.001
Coronary heart disease	11 (24.44 %)	19 (20.43 %)	0.145
Previous ischemic stroke	7 (15.56 %)	15 (16.13 %)	0.632

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

Chronic kidney disease	5 (11.11 %)	7 (7.53 %)	0.563
Chronic heart failure	5 (11.11 %)	3 (3.23 %)	<0.001
Hypertension	28 (62.22 %)	59 (63.44 %)	0.731

Laboratory parameters such as HDL, TG, FBS, HbA1c and Uric acid were deranged in diabetic patients as compared to non-diabetic patients and difference was statistically significant. While LDL and serum creatinine were comparable and difference was not significant statistically.

Table 3: Laboratory parameters

Parameters	Diabetic (n=45) (Mean ± SD)	Nondiabetic (n=93) (Mean ± SD)	P value
HDL (mg/dl)	34.98 ± 5.67	38.92 ± 6.92	<0.001
LDL (mg/dl)	161.2 ± 41.25	160.94 ± 42.97	0.41
TG (mg/dl)	169.75± 49.72	232.03 ± 71.78	<0.001
FBS (mg/dl)	156.02 ± 38.55	100.53 ± 12.35	<0.001
HbA1c(%)	8.08 ± 1.67	6.34 ± 0.82	<0.001
Sr. Creatinine (mg/dl)	1.65 ± 0.77	1.24 ± 0.59	0.46
Uric acid (mg/dl)	7.53 ± 0.82	6.25 ± 0.64	<0.001

On admission, National Institutes of Health Stroke Scale score at admission in diabetic patients (9.1 ± 7.8) was more as compared to non-diabetic patients (8.3 ± 7.2) and difference was statistically significant. Diabetic patients had more adverse outcome (53.33 % vs 20.43 %) and more in-hospital mortality (22.22 % vs 11.83 %) and difference was statistically significant. While duration of hospitalization (7.9 ± 5.1 days vs 7.7 ± 4.9 days) and modified Rankin Scale score at discharge (3.1 ± 2.7 vs 3.2 ± 2.8) were comparable and difference was not significant statistically.

Table 4: Outcome parameters

Parameters	Diabetic (n=45)	Nondiabetic (n=93)	P value
National Institutes of Health Stroke Scale score at admission	9.1 ± 7.8	8.3 ± 7.2	<0.001
Duration of hospitalization (d)	7.9 ± 5.1	7.7 ± 4.9	NS
Modified Rankin Scale score at discharge	3.1 ± 2.7	3.2 ± 2.8	NS
Adverse outcome (%)	24 (53.33 %)	19 (20.43 %)	<0.001
In-hospital mortality (%)	10 (22.22 %)	11 (11.83 %)	<0.001

Discussion

Stroke is one of the most frequent causes of death and disability worldwide with a significant clinical and socioeconomic impact. It has a heterogeneous etiology including unmodifiable risk factors such as genetic, age and sex, and modifiable risk factors including hypertension, diabetes mellitus, dyslipidemia, sedentary lifestyle, and smoking. [6]

Acute ischemic stroke (AIS) is the most common cause of mortality and long-term disability worldwide.[7] The risk of AIS is more than two-fold higher and more severe in patients with type 2 diabetes mellitus (T2DM).[8] It is associated with poorer functional outcomes and higher mortality risk.[9] About 40 to 60% of patients with AIS present with admission hyperglycemia either due to acute stress response or diabetes.[10]

The spectrum of neurological impairment following acute ischemic stroke is broad. The initial stroke severity predicts responses to treatment and outcomes after ischemic stroke. Favorable outcome after stroke was independently associated with younger age, a lower NIHSS score,

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

male gender.[11,12] In most of the ischemic strokes the underlying pathophysiology is atherosclerosis, which is a chronic inflammatory disorder in which immune mechanisms interact with modifiable metabolic risk factor like diabetes mellitus to initiate, activate and propagate vascular events.

When compared with non-diabetic patients, it is uncertain whether T2DM is independently associated with severe form of stroke and worse functional stroke outcome[13,14] or if this relationship was due to higher prevalence of Cerebrovascular disease (CVD) risk factors.[15]

Stress hyperglycemia in the early course of stroke is associated with a range of adverse effects like increased infection rates, independent of another prognostic factor, abnormal immune function and hemodynamic and electro cardiac abnormalities, and greater morbidity and mortality in acute ischemic stroke.[3,16]

Natuva SSN et al.,[17] noted that age, smoking, alcohol, CV Doppler, TGL, HDL, FPG, PPG and HbA1c were found to have cumulative influence on the stroke severity (NIHSS) and functional outcome (mRS). Whereas alcohol and HbA1C found to have significant independent predictive value for stroke severity at admission.

In study by Anitha S et al.,[18] among 195 patients of suspected stroke, T2DM was present in 54% of study population. Patient with T2DM had high NIHSS at admission; however mRS score at the time of hospital discharge did not differ statistically ($p < 0.05$). Patients with T2DM suffered a severe form of stroke than non-diabetics.

N Muralidhar[19] studied 200 cases of stroke, there was a high prevalence of CKD and CAD among non-diabetic stroke patients when compared to diabetic stroke patients. There was a significantly high prevalence of old CVA history among diabetic stroke patients (36%) when compared with non-diabetic group (16%) ($P = 0.003$). At admission, the NIHSS scores significantly differ between patients with T2DM of duration > 10 years ($n = 80$) from those patients with T2DM duration of < 10 years ($n = 20$) and patients without T2DM ($n = 100$), ($11.02 + 2.87$, 7.5 ± 2.8 and 7.12 ± 1.97, respectively; $P < 0.05$). The mRS score at discharge was significantly high in patients with T2DM duration of > 10 years, when compared to patients with T2DM duration of < 10 years ($2.75 + 1.36$ and 1.79 ± 0.98 respectively; $P<0.001$).

Knoflach M, et al.,[20] studied the association between prestroke glycemic control status and neurological or functional outcomes in 3,627 patients with first-ever ischemic stroke. It was suggested that the serum glycosylated hemoglobin (HbA1c) levels on admission was a significant independent predictor for clinical outcomes.

Lik-Hui Lau et al.,[21] conducted a meta-analysis of 39 studies (n = 359,783), estimated prevalence of diabetes was 28%. The rate was higher in ischemic (33%, 95% confidence interval 28–38) compared with hemorrhagic stroke (26%, 95% confidence interval 19–33) inpatients. Most, but not all, studies found that acute hyperglycemia and diabetes were associated with poorer outcomes after ischemic or hemorrhagic strokes: including higher mortality, poorer neurological and functional outcomes, longer hospital stay, higher readmission rates, and stroke recurrence.

Clustering of other risk factors like old age, smoking, alcoholism and dyslipidemia are observed in acute ischemic stroke patients with poor glycemic status. Estimation of HbA1c levels at the time of admission might be a predictor of the severity of neurological impairment and functional outcome in patients with acute ischemic stroke.[22] With achievement of near normal glycemic status in diabetic population the stroke severity and functional outcome levels can be brought to the same extent of that observed in non-diabetic population.

Conclusion

We report a high National Institutes of Health Stroke Scale score at admission, more adverse outcome more in-hospital mortality, in diabetic patients as compared to non-diabetic patients

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

and difference was statistically significant. Thus, type 2 diabetes does not appear to affect ischemic stroke severity but is associated with a worse functional outcome at discharge.

Conflict of Interest: None to declare
Source of funding: Nil

References

1. Victor M, Ropper AH, Adams RD, Ropper AH, Samuels MA. Cerebrovascular diseases. Adam‘s and Victor‘s Principles of Neurology. 9th ed. United States of America: McGraw Hill; 2009: 545–650
2. Luitse MJ, Biessels GJ, Rutten GE, Kappelle LJ. Diabetes, hyperglycaemia, and acute ischaemic stroke. Lancet Neurol 2012;11 (02):61–71
3. Lindsberg, P. J., and Roine, R. O. (2004). Hyperglycemia in acute stroke. Stroke, 35(2), 363-364
4. Harrison JK, McArthur KS, Quinn TJ: Assessment scales in stroke: clinimetric and clinical considerations. Clin Interv Aging 2013; 8: 201–211.
5. Air EL, Kissela BM: Diabetes, the metabolic syndrome, and ischemic stroke: epidemiology and possible mechanisms. Diabetes Care 2007; 30: 3131–3140.
6. Chaudhuri JR, Mridula KR, Alladi S, Umamahesh M, Balaraju B, Swath A, et al. Serum 25-hydroxyvitamin D deficiency in ischemic stroke and subtypes in Indian patients. J STROKE. 2014;16:44.
7. Mozaffarian D, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation. 2015;131(4):e29–322.
8. Luitse MJ, et al. Diabetes, hyperglycaemia, and acute ischaemic stroke. Lancet Neurol. 2012;11(3):261–71.
9. Tziomalos K, et al. Type 2 diabetes is associated with a worse functional outcome of ischemic stroke. World J Diabetes. 2014;5(6):939–44.
10. Gray CS, et al. Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK glucose insulin in stroke trial (GISTUK). Lancet Neurol. 2007;6(5):397–406.
11. Adams HP Jr, Leclerc JR, Bluhmki E, Clarke W, Hansen MD, Hacke W. Measuring outcomes as a function of baseline severity of ischemic stroke. Cerebrovasc Dis 2004; 18 :124-9.
12. Abanto C, Ton TG, Tirschwell Dl, Montano S, Quipse Y, Gonzales I, et al. Predictors of functional outcome among stroke patient in lima, Peru. J Stroke Cerebrovas Dis 2013; 12: 1052-3057
13. Luitse MJ, Biessels GJ, Rutten GE, et al. Diabetes, hyperglycaemia, and acute ischaemic stroke. Lancet Neurol 2012 Mar;11(3):261 71.
14. Mankovsky BN, Ziegler D. Stroke in patients with diabetes mellitus. Diabetes Metab Res Rev 2004 Jul-Aug;20(4):268 87.
15. Hatzitolios AI, Didangelos TP, Zantidis AT, et al. Diabetes mellitus and cerebrovascular disease: Which are the actual data? J Diabetes Complications 2009 Jul-Aug;23(4):283 96.
16. Davidson JA, Parkin CG. Is hyperglycemia a causal factor in cardiovascular disease? Does proving this relationship really matter? Yes. Diabetes Care. 2009 Nov;32 Suppl 2(Suppl 2):S331-3.
17. Natuva SSN, Tirupati S, Reddy AP, Vallampalli G, Gandra S. 2016. Independent Predictors of Severity and Functional Outcome of Acute Ischemic Stroke in Patients with Diabetes. J Neurol Exp Neurosci 2(1): 15-20.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

18. Anitha Silvery, MS Sreejit, Roney Thomas, et al. Association of Type 2 Diabetes with Severity and Functional Outcome of Acute Ischemic Stroke: A Prospective Observational Comparative Study. Indian J Emerg Med. 2020;6(1):9 13.
19. N Muralidhar. To study the Severity and Functional Outcome of Acute Ischemic Stroke patients with Type 2 Diabetes. J Adv Med Dent Scie Res 2021;9(10):10-14.
20. Knoflach M, Matosevic B, Rucker M, Furtner M, Mair A, Wille G, et al. Functional recovery after ischemic stroke: a matter of age: data from the Austrian Stroke Unit Registry. Neurology. 2012;78:279–285.
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. J Diabetes Investig. 2019 May;10(3):780-792.
22. Sunanda T, Kumar NSS, Reddy PA, Vallampalli G, Prasad PNS (2016) Role of HbA1c at Admission on Severity and Functional Outcome of Ischemic Stroke in Patients with Diabetes Mellitus. J Neurol Neurophysiol 7: 377.