Association of Type 2 Diabetes with Functional Outcome of Acute Ischemic Stroke: A Prospective Observational Comparative Study

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Abstract

Introduction: Ischemic stroke is an important non communicable disease worldwide. The number of patients suffering stroke due to Type 2 Diabetes Mellitus (T2DM) is expected to further increase with regards to the raising trend of T2DM. Due to the unequivocal association between T2DM and ischemic stroke, it is unclear whether patients with T2DM suffer severe forms of strokes or have worse functional outcome following stroke. *Aim of the study:* To evaluate the severity of stroke and its functional outcome in patients with T2DM. *Materials & method:* A prospective study was conducted on 195 patients of suspected stroke, fulfilling the inclusion criteria presenting to the emergency department of our institute during a period of 1 year. Diagnosis of stroke was made by symptoms at presentation and confirmed by CT/MRI brain scan. Data entry was done by Questionnaire on National Institute of Health Stroke Score (NIHSS) at the time of admission and Modified Ranking Stroke Score (mRS) at the time of discharge for each patient and analysis was done using Statistical Package for Social Sciences (SPSS version 20.0). *Results:* 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 ($p < 0.05$). *Conclusion:* Patients with T2DM suffered a severe form of stroke than non-diabetics.

Keywords: Acute ischemic stroke; NIHSS; mRS score; Type 2 DM.
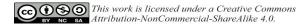

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Introduction

Stroke continues to be a leading cause of morbidity and mortality. A wide range of risk factors are associated with it. T2DM is a major independent risk factor for stroke.[1,2] T2DM accounts for 90–95% of all diagnosed cases of Diabetes mellitus.[3,4] Approximately T2DM had 2.27 times higher risk for ischemic stroke.[5] As there is raising prevalence of T2DM due to the epidemic of obesity, the number of patients suffering stroke due to T2DM is also expected to further increase. When compared with non-diabetic patients, it is uncertain whether T2DM is independently associated with severe form of stroke and worse functional stroke outcome[6,7] or if this relationship was due to higher prevalence of Cerebrovascular disease (CVD) risk factors.[8] The aim of this study is to compare the severity and outcome of acute ischemic stroke among the patients with T2DM and non-diabetics.

Materials and Methods

The Study was conducted prospectively on 195 patients who have reported to our Emergency Department after receiving the approval by the institution ethics committee. 195 patients were divided into 2 groups—Group A: Diabetic and Group B: Non-diabetic. Group A is further divided into Group A1: Controlled diabetic and Group A2: Uncontrolled diabetic based on the level of HbA1c. Patients with less than 9% HbA1c were categorized as controlled diabetic and more than or equal to 9% HbA1c were in uncontrolled diabetic group. Additionally the Group A was evaluated based on the duration of diabetes and divided into Group IA of diabetes less than 10 years and Group IIA of diabetes more than 10 years. Diabetic patients were defined in the study as self reported T2DM or those taking treatment for diabetes. All Patients presenting with symptoms of facial droop, arm drift, abnormal speech, sudden numbness or weakness of face, arm or leg, sudden confusion or aphasia and sudden visual deficits were included in the study. The presence of acute infarct was confirmed by MRI/CT brain. Those patients who satisfy the inclusion criteria were explained about the study and a written informed content was taken.

Inclusion criteria: Patients were considered to have acute ischemic stroke based on:

(1) Sudden onset of clinical symptoms of stroke.

(2) Presence of focal/global neurological deficits.

(3) Presence of an acute infarct as confirmed by either CT or MRI brain.

Exclusion criteria:

(1) Hemorrhagic stroke.

(2) Patients with severe left ventricular dysfunction, heart failure or acute myocardial infarction, which increases the mortality.

(3) Patients not willing for admission or routine investigation.

A standard structured questionnaire was completed by interviewing the patients. The questionnaire contained details of patient's age, sex, place of residence, date of arrival, date of discharge, presence of comorbidities like T2DM/hypertension (HTN)/chronic kidney disease (CKD)/coronary artery disease (CAD)/old cerebrovascular accident (CVA)/chronic obstructive pulmonary disease (COPD)/malignancy and their duration.

Neurological examination was done among both the sets of patients with NIHSS scale to assess the severity of stroke at the time of admission. NIHSS score range from 0-suggestive of no stroke to 42-which was suggestive of severe stroke. All the patients were admitted into medical wards or medical ICU's depending upon the clinical condition of the patient. Study groups were followed up during their hospital stay. Functional outcome including in hospital mortality at the time of discharge was assessed with modified rank in mRS scale which runs from 0–6 running from perfect health without symptoms to death. Adverse outcome was assessed by mRS score ≥ 2 or in hospital death.

Results

Among 195 patients, 115 were males and 80 were females with age ranging from 45 to 90 years. Comorbidities and risk factors in patients with and without T2DM among the acute ischemic stroke patients were assessed. There was a high prevalence of hypertension in diabetic group n = 89 (84.76%) as compared to non-diabetic stroke patients n = 73 (81.10%). However this was not statistically significant. There was a higher prevalence (23.80%) of COPD among the diabetic stroke patients when compared to non-diabetic group (15.55%). In the present study, 3.8% and 12.38% of diabetic group people were suffering from CKD and CAD respectively, where as in non-diabetic group, 7.77% and 14.44% of patients were suffering from CKD and CAD respectively. There was a high prevalence of CKD and CAD among non-diabetic stroke patients when compared to diabetic stroke patients. However, the prevalence was not statistically significant in between the two groups. There was a significantly high prevalence of old CVA history among diabetic stroke patients (35.23%) when compared with non-diabetic group (15.55%) p = 0.002. The lab characteristics of the two groups are depicted in Table 1. The severity and functional outcome in stroke based on NIHSS and mRS scores respectively are shown in the two groups in Table 2.

In the present study, univariate analysis was done using individual sample *t*-test to evaluate the association between T2DM duration with stroke severity and outcome. At admission, the NIHSS scores significantly differ between patients with T2DM of duration more than 10 years (n = 75) from those patients with T2DM duration of less than 10 years (n = 30) and patients without

T2DM (n = 90), (10.26 ± 3.1, 7.3 ± 2.9 and 7.0 ± 1.8, respectively; $p < 0.05$). The mRS score at discharge was significantly high in patients with T2DM duration of more than 10 years, when compared to patients with T2DM duration of less than 10 years (2.93 ± 1.25 and 1.84 ± 0.69 respectively; $p \leq 0.001$) (Tables 3 and 4).

Table 1: Lab characteristics

Characteristics	Group A Mean ± (SD)	Group B Mean ± (SD)	*p*-value
HDL (mg/dl)	35.07 ± 5.29	37.92 ± 5.33	<0.001
LDL (mg/dl)	160 ± 38.6	157 ± 27.35	0.551
TG (mg/dl)	216.41 ± 65.28	179.03 ± 45.5	<0.001
FBS (mg/dl)	133.52 ± 38.45	102.2 ± 12.46	<0.001
HbA1c(%)	7.80 ± 1.3	6.22 ± 0.41	<0.001
Sr. Creatinine (mg/dl)	1.52 ± 0.81	1.45 ± 0.57	0.506
Uric acid (mg/dl)	7.20 ± 0.64	6.32 ± 0.52	<0.001

(Mean = Mean Value; SD = Standard Deviation; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglycerides; FBS = fasting blood sugar; HbA1c = Glycosylated hemoglobin)

Table 2: Severity and outcome of stroke between Group A and Group B

Parameters	Group A Mean ± (SD)	Group B Mean ± (SD)	*p*-value
NIHSS score	8.02 ± 3.21	7.01 ± 1.88	0.009
mRS score	2.19 ± 0.97	2.15 ± 0.88	0.795
Duration of hospital stay (days)	6.5 ± 2.03	4.54 ± 1.47	<0.001
Rates of adverse outcome (%)	71.4	77.8	0.714

(Test used for above table is individual sample *t*-test)

Table 3: Univariate analysis using the individual sample t-test to evaluate the association between controlled and uncontrolled diabetics with respect to stroke severity and outcome

Parameters	Group A1 (*n* = 64)	Group A2 (*n* = 41)	*p*-value
NIHSS score Mean ± (S.D)	7.23 ± 2.58	9.7 ± 3.7	<0.001
mRS score Mean ± (S.D)	1.6 ± 0.64	3.0 ± 0.83	<0.001

(Group A1 = controlled diabetics; Group A2 = uncontrolled diabetics)

Table 4: Univariate analysis using individual sample *t*-test to evaluate the association between the groups based on duration of diabetes with respect to stroke severity and outcome

Parameters	Group IA (*n* = 30)	Group IIA (*n* = 75)	*p*-value
NIHSS score Mean ± (SD)	7.3 ± 2.9	10.26 ± 3.1	<0.05
mRS score Mean ± (SD)	1.84 ± 0.69	2.93 ± 1.25	<0.001

(Group IA = Diabetes of less than 10 years duration, Group IIA = Diabetes of more than 10 years duration)

Discussion

Diabetes mellitus is a major public health problem. Diabetes and ischemic stroke are the common diseases, which frequently occur together. Several studies[9-11] analyzed the relationship between these two disorders have shown that the subjects with diabetes mellitus have approximately twice the risk of ischemic stroke compared with non-diabetic patients. In our study, diabetes patients were younger, had a high body mass index, high prevalence of hypertension and recurrence of CVA. The present study findings were in accordance with a study conducted by Reeves[12] et al. in United

States where diabetes patients were younger, and had higher rates of previous cardiovascular disease, hypertension, and hypercholesterolemia. In the present study, there was a high prevalence of hypertension among diabetic patients when compared to the non-diabetic patients which was in accordance to a study conducted by Shashank R Joshi[13] et al. in India, where out of 7,212 patients with hypertension, diabetes was coincidental in 44.7% of patients.

Main finding of the present study was that the severity of ischemic stroke assessed with NIHSS was significantly (p = 0.009) differing between patients with T2DM and those without T2DM. A small study conducted on 50 diabetic patients by Kiers L et al.[14] was in accordance with the present study, suggesting that stroke is more severe in patients with T2DM. The abnormal metabolic state accompanying diabetes, result in changes in the arterial structure and function and may lead to high risk of ischemic stroke. A few studies have compared stroke severity between patients with T2DM and without T2DM, yielding conflicting results.[15,16] The two larger studies were conducted on 233 and 611 stroke patients with T2DM and reported no association between T2DM and stroke severity, which was in contrast with the present study findings.[16,17]

In the present study, mRS score at the time of discharge among the 2 groups was not statistically significant (p < 0.795). This was in accordance with the prospective study conducted by Tziomalos[15] et al. on 482 stroke patients which concluded that the mRS score at discharge did not differ between the two groups.

We also evaluated duration of diabetes and glycemic control amongst the diabetic patients and compared these verity and functional outcome in between these groups. In univariate analysis, the stroke patients with duration of diabetes >10 years had a significantly (p = <0.001) high mRS score when compared to the stroke patients with diabetes duration ≤ 10 years. Uncontrolled diabetic patients were associated high mRS score and was statistically significant (p = <0.001) indicating a poor functional outcome in acute ischemic stroke patients with poorly controlled glycemic levels. This finding in the present study was in accordance with a study conducted by Kiers[14] et al. on 176 patients with acute stroke. They have concluded that stress hyperglycemia and uncontrolled diabetic were associated with poor stroke outcome.

The rates of adverse outcome at discharge did not differ between diabetic and non-diabetic patients (p = 0.714). But from the previous studies[18–20] it is understood that diabetes is a common comorbidity in stroke patients and is associated with poor outcomes after stroke. In our study the adverse outcome was higher in patients with diabetes (71.4%) which is in contrast to a study conducted by Reeves[12] et al. in United States where diabetes had important independent associations with adverse stroke outcomes. The present study results may be because of other confounding factors like smoking and alcohol consumption, which were more in non-diabetic patients.

Conclusion

Present study found that the severity of ischemic stroke as assessed by NIHSS score was significantly high among the patients with T2DM than those without T2DM indicating that diabetics suffered a severe form of stroke. Short-term functional outcome of acute ischemic stroke as measured by modified Rankin stroke scale (mRS) did not differ between the two groups. Though the prevalence of comorbidities like HTN, COPD, CAD was high in diabetic group, the comorbidities in diabetic and non-diabetic group was not statistically different. Hence it is understood that diabetes may probably be an independent risk factor that may be associated with severe form of stroke. Health education programs should be conducted to educate the people regarding prevention of diabetes by lifestyle modification. There is a need to conduct follow up studies with longer duration to know the causal association between diabetes and stroke. The needs of diabetic patients are not only limited to adequate glycemic control but also correspond with preventing complications; disability limitation and rehabilitation. Patients with type 2 diabetes are advised to monitor the cerebrovascular risk factors like lipid profile in the blood, BMI, glycemic condition to prevent the cerebrovascular diseases among them. There is a need for regular follow-up of diabetic patients with the health care provider in averting long-term complications.

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