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Comparative evaluation of diabetic and non-diabetic stroke and the study of the effect of glycemic levels on the outcome of strokes

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Abstract
Background: Diabetes potentiates stroke by favoring thrombosis and atherogenesis by various mechanisms. Clinical profile of stroke is different in diabetics compared in non-diabetics in many aspects.
Methods: To study and compare the clinical profile of stroke in diabetics and non-diabetics.
Results: Stroke patients in both study groups presented with history of motor weakness as their most common presenting complaint (90% in both groups had hemiparesis/hemiplegia and 10% had monoparesis/monoplegia).
The mean HDL cholesterol was 35.97 mg/dl in the diabetic group and 43.27 mg/dl in the non-diabetic group. The mean LDL cholesterol was 108.97 mg/dl in the diabetic and 119.90 mg/dl in the non-diabetic group. The mean triglycerides was 183.77 mg/dl in the diabetic and 142.77 mg/dl in the non-diabetics.
63.3% of diabetics had 33.3% of non-diabetics had infarction on CT Brain. 36.7% of diabetics and 66.7% of non-diabetics had hemorrhage on CT Brain.
In the diabetic group; patients with a fair recovery had a mean RBS of 174.91 mg/dl while patients with poor recovery had a mean RBS of 216.56 mg/dl. In the non-diabetic group; patients with a fair recovery had a mean RBS of 115.12 mg/dl, patients with poor recovery had a mean RBS of 147.00 mg/dl.
Conclusion: Stroke in diabetes was noticed by increase in mortality and morbidity; severity of stroke was more in diabetic and rehabilitation was delayed. Moreover recurrent stroke was more common in diabetics Hyperglycaemia at stroke onset was associated with higher risk of poor outcome independent of the other variables.

Keywords: diabetes, stroke, hyperglycemia

Introduction
World Health Organization 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 origin [1].
The majority (about 80%) of stroke is ischemic; the remainder result from primary hemorrhage either intracerebral or subarachnoid space. Ischemic stroke is often thought as a single entity but, in fact it may be the result of quite different disease processes [2, 3].
Diabetes mellitus is a risk factor for both an increased incidence of and mortality from stroke [4]. The first edition of Diabetes in America documented the strong association of diabetes with risk of stroke, especially strokes due to vascular disease and infarction [5].
In the Multiple Risk Factor Intervention Trial (MRFIT) in 1973-75, 12-year mortality was determined for 5,163 men aged between 35-57 years who reported taking medication for diabetes and 324,815 men without a history of diabetes [6].
The improved clinical diagnosis of stroke by computerized tomography and magnetic resonance imaging has probably increased the measured incidence of stroke in the population, especially among older individuals who receive more frequent and intensive medical care. Further, there is probably a very high prevalence of "silent" cerebral infarction that can be documented by these new noninvasive techniques. The incidence and prevalence of stroke among diabetic patients may, therefore, be higher now than was suggested in the past.
The incidence of stroke also increases with increasing age. Thus, many stroke patients may have undetected diabetes at the time of the stroke; subsequent examination in the hospital or following treatment for stroke may identify the previously undetected diabetes. The reported prevalence of diabetes among stroke patients as compared with those without a stroke may therefore be inflated by differences in ascertainment.
Diabetes potentiates stroke by favoring thrombosis by increasing concentration in blood of prothrombotic factors like fibrinogen and von Willebrand factor. It also increases platelet adhesiveness. Fibrinolytic capacity is decreased through increased concentrations of plasminogen activator inhibitor type 1.
Diabetes also favours atherogenesis because of various lipid abnormalities like hypertriglyceridemia, low HDL cholesterol and high triglyceride-enriched HDL. Glycosylation of lipoproteins and oxidation of lipoproteins leads to atheroma formation.
The relative risk of stroke in diabetics approximately doubled compared to with that in patients without diabetes. Clinical profile of stroke is different in diabetics compared in non-diabetics in many aspects. Intracerebral hemorrhages are less frequent in diabetic patients whereas lacunar infarcts are more

frequent in diabetics.

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 [7, 8, 9, 10, 11, 12].

The present study was undertaken in a prospective manner to comparatively evaluate stroke in diabetic and non-diabetic patients and to study the effect of glycemic levels on the outcome of strokes.

Material and methods

Aim and objectives

- To study and compare the clinical profile of stroke with respect to age, sex, stroke type, stroke severity, prevalence of risk factors, and outcome in diabetics and non-diabetics.
- To study and correlate the effect of admission glucose levels on the outcome of diabetic and non-diabetic strokes.

Methodology

The present study was a case control observational study. This study was conducted on 60 patients with stroke (out of which 30 patients were diabetic or found to have diabetes, and 30 were non-diabetic stroke patients) admitted to Meenakshi Medical College & Research Institute, Enathur, Kanchipuram. Patients who were admitted with history of acute stroke and confirmed by thorough physical examination and CT BRAIN to have stroke, and were satisfying the inclusion and exclusion criteria were studied.

Inclusion criteria

1. All stroke patients with diabetes (cases).
2. Diabetes was 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 underwent repeat blood sugar (48 hours after admission) and HbA1C estimation. Those satisfying WHO criteria were labeled as newly detected diabetics and included as cases otherwise were labeled as stress hyperglycemics and included as controls.

Exclusion criteria

1. Patients receiving diabetogenic drugs.
2. Patients having severe stroke who died before it could be established whether they had diabetes or not.
3. Patients with severe stroke who died before it could be established whether they had stroke or not.
4. All uncommon strokes caused by hypercoagulable disorders, venous sinus thrombosis, vasculitis etc.

After admission detailed history regarding temporal profile of stroke and risk factors like hypertension, diabetes mellitus, smoking, alcohol intake, previous strokes were taken.

Detailed neurological examination was done and stroke score based on MRC scale was obtained during admission. Three stroke severity categories were developed.

Mild	= 4
Moderate	3 - 2
Severe	1 - 0

Stroke score based on MRC (Medical Research Council) scale

Grade 0:	No contraction
Grade 1:	Flicker of contraction
Grade 2:	Active movement with gravity eliminated
Grade 3:	Active movement against gravity
Grade 4:	Active movement against gravity and moderate resistance
Grade 5:	Active movement against gravity and full resistance (normal power).

Prognosis of these patients were assessed on the basis of improvement or deterioration based on MRC scale.

Simple hierarchal scale was used to assess upper and lower limb qualitative function on admission and after 6 weeks. Patients were graded according to best unassisted functional outcome achieved as below

Upper limb

1. Normal
2. Fasten button
3. Hold cup
4. No use

Lower limb

1. Normal
2. Climb stairs
3. Walk on flat surface
4. Stand
5. No use

Neurological outcome after 6 weeks was graded as follows

Good: Patients who can return to normal or previous activities, mild hemiparesis, mild dysphasia (MRC=4)

Fair: Patients who were independent in activities of daily living but were unable to return to previous activities, moderate paresis, moderate dysphasia (MRC 3-2)

Poor: Patients who were dependent on others for daily living activities, severe paresis to plegia, aphasia (MRC 1-0).

This assessment was done immediately after admission and it was repeated after 6 weeks in survivors. Patients were categorized as dead or survived with or without improvement.

The following investigations were done in all the cases

1. Complete hemogram
2. RBS on admission
3. FBS (48 hours after admission)
4. HbA1C
5. Blood Urea/ Serum Creatinine
6. ECG
7. Lipid profile (including total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol).
8. CT Scan Brain

9. PT & APTT

Results

The mean age in diabetic stroke patients was 56.33±10.049 yrs. and in non-diabetic stroke patients was 59.63±13.061yrs. Maximum patients were in the age group 51-60 years (46.7%) in diabetic group and in the above 60 years age group (50%) in non-Diabetic group.

Difference in mean age in study was not statistically significant.

Out of 30 diabetic stroke patients 22 were males and 08 were females where as in non-diabetics 21 were males and 09 were females. Percentage of male population in both the groups was higher.

Stroke patients in both study groups presented with history of motor weakness as their most common presenting complaint (90% in both the groups had hemiparesis/hemiplegia and 10% had monoparesis/monoplegia).

60% in the diabetic group and 63.3% in the non diabetic group were alert, while 16.7% in diabetic and 13.3% in non diabetic were responding to painful stimuli, 10% of diabetic and non diabetic patients were unconscious, 13.3% of both diabetic and non diabetic people were responding to verbal command as seen in Figure 1.

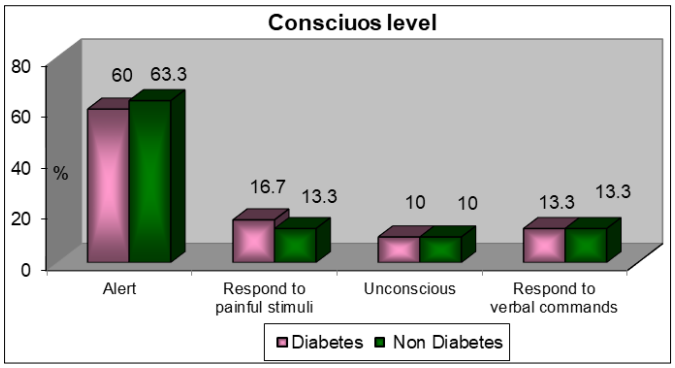

Fig 1: Conscious Level in diabetic and non diabetic stroke

Speech disorder was present in 23.3% of diabetics and 26.7% of non diabetics. History of cranial nerve involvement was in 26.7% of both the group of patients. Visual disturbance was present in 10% of diabetic patients. Other complications like convulsion was present in 10% of diabetics and 6.7% of non diabetics.

53.3% of diabetic stroke patients and 43.3% of non-diabetic stroke patients had no history of addictions in the past. History of tobacco chewing was 10% in diabetics and 6.7% in non-diabetics. Alcoholism was 16.7% in diabetics and 26.7% in non-diabetics. Smoking was 20% in diabetics and 23.3% in non-diabetics. Smoking and alcohol consumption was more frequent in the non-diabetic group.

The mean systolic blood pressure on admission was 148.10± 20.10mmHg in diabetic group and 158.07±11.172mmHg in non-diabetic group. The difference was statistically significant. The mean diastolic blood pressure on admission was 91.57±11.602 mmHg in diabetic group and 95.73±7.423mmHg in non-diabetic group. The difference was statistically insignificant.

The mean HDL cholesterol was 35.97± 8.282mg/dl in the diabetic group and 43.27±11.039mg/dl in the non-diabetic group. The mean LDL cholesterol was 108.97±40.586mg/dl in the diabetic and 119.90±37.534mg/dl in the non-diabetic group. The mean triglycerides was 183.77 ± 86.742mg/dl in the diabetic and 142.77± 38.518mg/dl in the non-diabetic group. Total Cholesterol was 179.27 ± 48.141mg/dl in the diabetic and 189.03 ± 41.139mg/dl in the non-diabetic group. Mean triglycerides was higher in the diabetic group and mean HDL was lower in diabetic group as compared to the non-diabetic group. Both the values were statistically significant.

63.3% of diabetics and 33.3% of non-diabetics had infarction on CT Brain. 36.7% of diabetics and 66.7% of non-diabetics had hemorrhage on CT Brain.

Hemorrhagic strokes were more frequent in the non-diabetics and ischemic strokes in the diabetic stroke groups. The difference was statistically significant. Likelihood ratios were 0.004 and 0.00, which were highly significant.

Diabetic stroke patients had longer duration of hospital stay 10.00 ± 4.251 days compared with non-diabetics 7.40 ±4.199 days. The difference was statistically significant.

36.7% had fair recovery in diabetic group as compared to 83.3% in non-diabetic group. 53.3 % had poor recovery in diabetic and 6.7% had poor recovery in non-diabetic group. Death was seen in 10% of patients in both the groups. Overall outcome was better in the non-diabetic stroke patients.

In the diabetic group; patients with a fair recovery had a mean RBS of 174.91±35.812mg/dl while patients with poor recovery had a mean RBS of 216.56±76.345mg/dl, patients who died had a mean RBS of 309.00±79.831mg/dl. In the non-diabetic group; patients with a fair recovery had a mean RBS of 115.12± 25.294mg/dl, patients with poor recovery had a mean RBS of 147.00±52.326mg/dl, and patients who died had a mean RBS of 215.33± 5.774mg/dl. Overall in both the groups patients with a higher admission RBS value had a poor outcome as mentioned in Figure 2. The difference was statistically significant in both the groups.

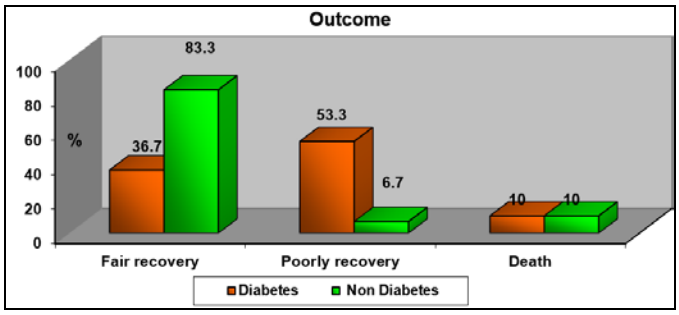

Fig 2: Association between outcome and RBS in diabetic and non diabetic stroke

Discussion

The present study involved 60 patients who satisfied the inclusion and exclusion criteria out of which, 30 were diabetic stroke patients and 30 non-diabetic stroke patients. Out of the 30 diabetic stroke patients 26 were known diabetics and 4 were detected to have type 2 diabetes during hospital stay.

Age incidence

In the present study, the mean age in Diabetic stroke patients

was 56.33±10.049. And in Non-Diabetic stroke patients was 59.63±13.061. Maximum patients were in the age group from above 60(38.3%) in Diabetic stroke 51-60 years (46.7%) and above 60(50%) in Non-Diabetic group.
In the Copenhagen Stroke Study [13], the diabetic stroke patient was 3.2 years younger than the nondiabetic stroke patient (P < .001). The observation in the present study, that Stroke occurs at a younger age in diabetics (56.33±10.049yrs) than in non-diabetics (59.63±13.061yrs) was similar to earlier studies.

Sex distribution
The observation in the present study, that men were at greater risk for stroke in both the diabetic and non-diabetic group was similar to the studies done by Zafar A *et al.* (2007) [14] and Kamel A *et al*. (2006) [15]. Our observation was contrary to that by Seppo Lehto, *et al*. 1996 [16], who found women at greater risk for stroke than men.

Presenting complaints
Stroke patients in both study groups presented with history of motor weakness as their most common presenting complaint (90% in both the groups had hemiparesis/hemiplegia and 10% had monoparesis/monoplegia). History of cranial nerve involvement was present in 26.7% in both the group of patients. Visual disturbance was present in 10% of diabetic patients. Speech disorder was present in 23.3% of diabetics and 26.7% of nondiabetics. Altered sensorium was present in 40% of diabetics and 36% of non-diabetic patients. Other complications like headache and unsteadiness of gait was present in 10% of diabetics and 7% of nondiabetics.

Risk factors for stroke
a. Previous history of hypertension
The observation in the present study, that previous history of hypertension was more common in the diabetics (70%) than in the non-diabetics (33.3%) was similar to the studies by Sarkar RN [17] *et al*., Zafar A [14] *et al*. (2007), Kamel A [15] *et al*. (2006) and Megherbi SE [18] *et al*. (2003). Similar results were also found by Kiessla BM [19] *et al*. 2005 and in the Copenhagen Stroke Study [13].

b. Previous history of ischemic heart disease
The observation in the present study, that previous history of ischemic heart disease was more common in the diabetics (26.7%) than in the non-diabetics (6.7%) was similar to the studies by Zafar A [14] *et al*. (2007) and Kamel A [15] *et al*. (2006).

c. Previous stroke
In the present study, previous history of CVA was more common in the diabetic group (36.7%) which was similar to the study by Sarkar RN [17] *et al*. and is contrary to the study by Zafar A [14] *et al*. (2007) which found similar incidence in both the groups.

Personal history
The observation in the present study, that current or previous smoking was distributed equally between the 2 groups (approx. 20%), but alcohol consumption was low in the diabetic group (16.7% vs 26.7%) was similar to the results of the study by Megherbi SE [18] *et al*. (2003).

Blood pressure on admission
The observation in the present study, that mean systolic and diastolic blood pressure on admission was higher in the non-diabetic (mean S.B.P 158.07±11.172mmHg and mean D.B.P 95.73±7.423mmHg) than the diabetic group (mean S.B.P 148.10± 20.10mmHg and mean D.B.P 91.57±11.602mmHg), was contrary to the study done by Kamel A [15] *et al*. (2006). Diabetics were under treatment for hypertension as compared to non-diabetics, which could be the explanation for low blood pressure on admission in diabetics than non-diabetics.

Glycemic status on admission
The observation in the present study, that admission RBS was higher in the diabetic group (210.53±73.491mg/dl) than in the non-diabetic group (127.27±39.781mg/dl) was similar to the study done by Kamel A [15] *et al*. (2006).

ECG
50% of diabetic stroke patients and 63.3% of non-diabetic stroke patients had normal ECG. 16.7% of diabetics and 23.3% of non-diabetics had LVH. 20% of diabetics and 6.7% of non-diabetics had ischemia.13.3% of diabetics and 6.7% of non-diabetics had infarction.

Stroke type
In the present study, 63.3% of diabetics had 33.3% of non-diabetics had infarction on CT BRAIN. 36.7% of diabetics and 66.7% of non-diabetics had hemorrhage on CT BRAIN. Hemorrhagic strokes were more frequent in the non-diabetics and ischemic strokes in the diabetic stroke groups.
In the study by Sarkar RN [17] *et al*. ischaemic stroke were higher in diabetic group (69%) as compared to non- diabetic group (45.8%).Haemorrhagic stroke was higher in non-diabetic group (52.7%) than in diabetic group (30.4%). In the Copenhagen Stroke Study [13], intracerebral hemorrhage was six times less frequent in diabetic patients.

Duration of hospital stay
Duration of hospital stay was longer in diabetic than in the non-diabetic group. The mean duration of hospital stay was 10.00±4.251 days in diabetic and 7.40 ±4.199 days in the non-diabetic group.
Control of blood sugar and treatment of other complications in diabetic subjects like hypertension, ischemic heart disease, diabetic nephropathy took longer time and was the cause of longer stay in the hospital.

Lipid profile
In the present study, diabetic patients had higher mean triglycerides (183.77± 86.742mg/dl Vs 142.57±37.518mg/dl) and lower HDL (35.97±8.282mg/dl Vs 43.27±11.039mg/dl) as compared to non-diabetic group. Kamel A [15] *et al*. (2006) found higher triglycerides in the diabetic group (211.6±80.2mg/dl Vs 166.5±35.8mg/dl) as compared to the non-diabetic group. Seppo Lehto [16] *et al*. 1996 also observed hypertriglyceridemia and low HDL in diabetic stroke patients.
Stroke outcome
In the present study, stroke patients with diabetes had a poor

outcome compared to stroke patients without diabetes. Similar observations were made by Megherbi SE [18] *et al*. (2003), Kamel A [15] *et al*. (2006) and in the Copenhagen Stroke Study [13].

Hyperglycemia on admission and outcome

In the present study, patients with high admission blood sugar had a poorer outcome as compared to those with lower blood sugar values in both the diabetic and non-diabetic study groups. Similar observations were made by McCall [20] *et al*. and Fuentes B [21] *et al*. In the Copenhagen Stroke Study [13], increased glucose levels on admission independently increase mortality from stroke in nondiabetic but not in diabetic patients.

Conclusion

In this study commonest modifiable risk factors in stroke were diabetes mellitus, hypertension, smoking, Dyslipidemia and alcohol consumption. Commonest non modifiable risk factors were increasing age, male sex and family history of stroke.

Diabetes was an independent risk factor for stroke. Stroke in diabetes differed from that of stroke in non-diabetics with respect to age, sex, stroke type, stroke severity, prevalence of risk factors, and outcome. Stroke in diabetes was noticed by increase in mortality and morbidity; severity of stroke was more in diabetic and rehabilitation was delayed. Moreover recurrent stroke was more common in diabetics.

Early diagnosis, treatment including lifestyle modification and prevention of diabetes may reduce the development of stroke and its complications and it presents a major challenge for health care professionals facing an epidemic of both diabetes and stroke.

Hyperglycaemia at stroke onset was associated with higher risk of poor outcome independent of the other variables.

Treatment or prevention of modifiable risk factors can reduce the mortality and morbidity of stroke.

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