

Comparative Study of Ischemic Stroke Outcome in Diabetic Patients Versus Non-Diabetic Patients

Basam Venugopal¹, Matta Gopi Srikanth², NS Sampath Kumar³

Abstract

Context: Stroke is one of the major disorders associated with severe morbidity and mortality. Diabetes is associated with occurrence, poor outcome and also chance of recurrence in stroke patients.

Aims: The present study was aimed to identify the severity of stroke among diabetics and how it differs from non diabetics and also to evaluate the outcome of acute ischemic stroke among diabetics and non diabetics for a short course of three and six months period.

Settings and Design: A prospective observational cross sectional study for one year period was conducted by Neurology department after ethical approval on cases of acute ischemic stroke.

Materials and Methods: Cases were divided into diabetics and non diabetics and socio- demographic data, risk factors were noted and severity of the stroke was assessed by using National Institute of Health stroke scale at the time of admission and Grouped into four based on the score. Outcome of the cases was categorized as dependent/ death and independent and placed in two groups based on modified Rankin score (mRS). Follow up of the cases was done for third and sixth month. Analysis was done by Microsoft excel and Probability values <0.01 were considered significant.

Results: 300 cases of acute ischemic stroke with 198 males, 102 females and 108 (36%) diabetics and 192 non diabetics (64%) were included. 60-69 years was the most common age group (34%), 62.7% were admitted in <24 hours. Majority of the cases were placed in Group 2 and statistical significance was associated with prognosis among diabetics and non-diabetics. The mortality percentage at the end of third and sixth month in the overall study group was 5.3% and 7.04%.

Conclusion: To conclude, our study found a significant association between diabetes and severity of stroke with NIHSS scoring as a tool of predictor in severity. Diabetes increased the risk of severity of stroke and dependent outcome among the acute ischemic stroke patients.

Keywords: Acute Ischemic stroke; Diabetics; Modified Rankin score; NIHSS.

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Introduction

Stroke is one of the major disorders associated with severe morbidity and mortality. The two types of stroke are ischemic stroke due to thrombosis, embolism and systemic hypoperfusion and hemorrhagic stroke due to subarachnoid or intracerebral haemorrhage. Approximately 80 percent of strokes are due to ischemic cerebral infarction and 20 percent to brain haemorrhage. Association of risk factors like hypertension,

diabetes increases the morbidity and affect the outcome of cases with stroke. Among various risk factors diabetes is associated with occurrence, poor outcome and also chance of recurrence in stroke patients. Chances of stroke are increased with advanced age in diabetics.¹ Diabetes mellitus is a very common metabolic disorder with a high and increasing prevalence worldwide affecting an estimated 415 million people globally in 2015, and is predicted to affect 642 million people by 2040. India tops the list with the largest number of diabetic persons (57 millions in 2010) which is expected to rise to 90 millions in another 20 years.^{2,3} Despite India one of the country with high number of diabetes cases, the association of diabetes with severity and outcomes in relation to stroke are limited and different. Hence the present study was aimed to identify the severity of stroke among diabetics and how it differs from non diabetics. The study also aims to evaluate the outcome of acute ischemic stroke among diabetics and non diabetics for a short course of three and six month period.

Materials and Methods

The present hospital observational study was conducted at Department of Neurology of a tertiary care hospital for a period of one year from January 2016 to December 2016. The study was presented to the institutional ethical committee and was approved. The study was conducted as per the guidelines of the committee. All the cases of stroke attending the neurology or emergency department of the hospital and diagnosed as acute ischemic stroke were included in the study. Patients with cerebral contusions, valvular heart disease, intracerebral, subdural, epidural and subarachnoid haemorrhage and less than 18 years of age were excluded from the study. Socio demographic data, social variables, past history of stroke and total history of diabetes (Duration, type, medications etc) and other risk factors like hypertension, smoking, and alcoholism were noted in a separate predesigned structured questionnaire by interviewing the case in the study or by previous medical records. Routine biochemical investigations like fasting blood sugar, serum lipid profile, Hb1Ac (Glycosylated Haemoglobin), Haemogram, renal function tests and serum electrolytes were done in all the cases in the study. Chest X-ray, 12 leads electrocardiography, echocardiography (2D mode and M mode) were performed to for all patients quantify the cardiac function and to rule out any valvular heart disease. CT and MRI imaging were

done in cases to confirm acute ischemic stroke.

Blood sugar estimation was done at the time of admission and all the cases were divided into diabetic and non diabetic cases. A patient was confirmed for diabetes if he or she had a known history of type 2 diabetes mellitus (DM), and glucose levels were >110 mg/dl. In case of those without known DM, the admission blood glucose was \geq 150 mg/dl. The severity of Acute Ischemic stroke (AIS) was evaluated using the National Institute of Health stroke scale (NIHSS). The NIHSS score consists of 15 items with a score of 1–42 points. Score of 0 = no stroke, 1–6 = minor stroke, 7–18 = moderate stroke, 19–42 = severe stroke. The Modified Rankin Scale (mRS) was used for evaluating outcome.⁴ Based on mRS the patients were grouped into two outcome groups – improved groups (mRS score 1-3), dependent/expired group (MRS score 4-6).

Follow up study: At 3 and 6 months after stroke onset respectively, the follow up of cases in terms of outcomes were assessed through telephonic conversation.

Statistical analysis: The collected data was entered in Microsoft excel spread sheet and analyzed for any corrections. The baseline variables were expressed in terms of number and percentage and its association with study groups was determined by using chi-square test. The data on continuous variables was summarized in terms of mean and SD. Probability values <0.01 were considered significant.

Results

In the present prospective hospital cross sectional study, a total of 300 cases of acute ischemic stroke confirmed by imaging and fulfilling the inclusion criteria were included. 198 cases (66%) were males and females 102 cases (34%) with a male to female ratio of 1.94:1. Of the 300 cases included in the study, 108 (36%) were diabetics and 192 (64%) were non diabetics. Of the 108 diabetics, 68 (63%) were males and 40 cases (37%) were females. The most common age group in the study was 60–69 years with 102 cases (34%) followed in order by 50–59 years (29.3%), >70 years (17.3%), 40–49 years (15%) and least was 30–39 years with 4.3%. The mean age of the patients in the study was 59.26 ± 6.24 with age range of 33–80 years. 108 cases (36%) in the study had diabetes, 130 cases (43.3%) were hypertensive with more prominence on systolic BP, 143 (47.66%) were chronic smokers, 137 cases (45.66%) were alcoholics and 28 cases (9.33%) had coronary heart

Table 1: Age and risk factor distribution among the cases in the study

	No.	Percentage (%)
Age (Years)		
30-39	13	4.3
40-49	45	15.0
50-59	88	29.3
60-69	102	34.0
>70	52	17.3
Total	300	
Risk Factors		
Diabetes	108	36
Hypertension	130	43.3
Smoking	143	47.7
Alcoholism	137	45.7
CAD	28	9.3
Atrial Fibrillation	1	0.3
Valvular disease	7	2.3
Time of admission		
Admission <24 hrs	188	62.7
Admission between 24-72 hrs	112	37.3

disease (CAD). Of 108 cases of diabetes, 77 had associated hypertension. 188 cases (62.7%) were admitted in less than 24 hours of acute ischemic stroke and 112 cases (37.3%) after 24 hours and before 72 hours. 82 cases admitted before 24 hours were diabetics and 106 were non diabetics (Table 1).

Based on NIHSS score, all the cases were categorized in to four groups (Group 1-NIHSS score 1-7; Group 2-NIHSS score 8-12; Group 3-Score 13-16; Group 4-NIHSS score 17-42.) (Table 2) summarizes the distribution of cases based on

the gender and risk factors depending upon the National institute of health stroke scale [NIHSS] at the time of admission. Majority of the cases were placed in Group 2 (NIHSS Score 8-12) None of the factors were found to be statistically significant except Hb1Ac. (p -value <0.001)

Table 3 explains the distribution of cases as per the age and their distribution as per the NIHSS score during admission. Majority of cases (115/300; 38.34%) in the study were in Group 2 with NIHSS score of 8-12. There was no statistically significant

Table 2: Distribution of cases based on NIHSS score on admission and Gender & Characters

Character & Factor	NIHSS (1-7)	NIHSS (8-12)	NIHSS (13-16)	NIHSS (17-42)	p -value
Gender					
Male	52	83	45	18	0.264999
Female	30	31	29	12	
Hypertension					
YES	34	57	27	12	0.399221
No	48	59	46	17	
Smoking					
YES	28	58	45	15	0.011081
No	53	59	29	13	
Alcohol					
YES	30	58	36	13	0.293496
No	50	65	32	16	
2D ECHO					
LVH	12	17	13	5	0.953121
Normal	70	97	63	23	
Hb1Ac (Glycosylated Haemoglobin)					
≥ 6.5	6	19	56	20	0.0001
< 6.5	78	99	18	4	

NIHSS: National Institute of Health stroke scale

association between age distribution and NIHSS score in the present study.

Table 4 explains the comparison of NIHSS score among diabetics and Non diabetics. Majority of the diabetics during admission were placed in the group

-3 with NIHSS score of 13-16. (65/108) and majority of Non diabetics were in Group 2 with NIHSS score of 8-12 (103/192). There was statistically significant association with diabetics and non diabetics and NIHSS score in the present study. (p -value <0.0001)

Table 3: Age wise distribution of cases and NIHSS Score at admission

Age (Years)	NIHSS (1-7)	NIHSS (8-12)	NIHSS (13-16)	NIHSS (17-42)	p -value
30-39	6	4	1	2	0.092899
40-49	16	20	8	1	
50-59	23	30	30	5	
60-69	27	41	22	12	
>70	11	20	12	9	
Total	83	115	73	29	

Table 4: NIHSS at admission in Diabetics vs Non diabetic cases in the study

Admission	Diabetics	Non-diabetics	Total	p -value
NIHSS (1-7)	5	78	83	<0.00001
NIHSS (8-12)	12	103	115	
NIHSS (13-16)	65	8	73	
NIHSS (17-42) including Deaths	26	3	29	
Total	108	192	300	

Table 5: NIHSS at discharge in Diabetics vs Non diabetic cases in the study

Admission	Diabetics	Non-diabetics	Total	p -value
NIHSS (1-7)	8	185	193	<0.00001
NIHSS (8-12)	81	7	88	
NIHSS (13-16)	19	0	19	
NIHSS (17-42) including Deaths	0	0	0	
Total	108	192	300	

(Table 5) explains the comparison of NIHSS score among diabetics and non diabetics at the time of discharge. There was statistically significant difference in the prognosis of non diabetics than diabetics. Majority were in the Group 1 at the time of discharge with NIHSS score of 1-7.

Follow up Study

Based on mRS scoring, the cases were divided into two groups, Group 1 with mRS score (1-3)

improved and mRS score (4-6) dependent/expired Group 2. Of the 108 diabetic cases, 48 cases (44.44%) were placed in Group 1 and 60 cases (55.56%) in Group 2 at the end of three months. Of 60 cases in Group 2, 12 cases had death as the outcome. 146 cases of non diabetics (76.04%) were in Group 1 and 46 cases (23.96%) in Group 2 at the end of 3rd month. Of the 46 cases in Group 2, 4 cases had death as final outcome. The mortality percentage at the end of third month in the overall study group was 5.3%.

Table 6: Results of follow up of cases in the study as per mRS (Modified Rankin score) score

Duration of follow up		No	%
Three months follow up	Group 1 [mRS score (1-3)]		
	Diabetics	48	44.44
	Non diabetics	146	76.04
	Group 2 [mRS score (4-6)]		
	Diabetics	60	55.56
	Non diabetics	46	23.96

Duration of follow up		No	%
Six months follow up	Group 1 [mRS score (1-3)]		
	Diabetics	58	60.42
	Non diabetics	154	81.91
	Group 2 [mRS score (4-6)]		
	Diabetics	38	39.58
	Non diabetics	34	18.09

By the end of six months, of the 96 cases of diabetics, 58 cases (60.42%) were placed in Group 1 (mRS score 1-3) and 38 cases (39.58%) in Group 2 (mRS score 4-6). Twelve cases of Group 2 in diabetics recorded death as the final outcome. Among the 188 cases of non diabetics, 154 cases (81.91%) were placed in Group 1 (mRS score 1-3) and 34 cases (18.09%). Of the 34 cases in Group 2, 8 cases had death as final outcome. The mortality percentage at the end of sixth month in the overall study group was 7.04% (Table 6).

Discussion

Ischemic stroke is a heterogeneous pathophysiological entity in which vastly different pathways might lead to indistinguishable clinical presentations. Well recognized mechanisms of ischemic stroke include cardiac or artery-to-artery embolism, atherothrombosis of an extra-cranial carotid or intracranial artery due to Type 2 DM, and various independent risk factors like hypertension, dyslipidemia, non-atherosclerotic disease of small-diameter penetrating arteries. However, it is generally accepted that atherosclerosis of extra-cranial or intracranial arteries due to Type 2 DM accounts for a substantial proportion of clinical ischemic strokes. Type 2 DM studied in the context of coronary disease, are assumed to be determinants of ischemic stroke.

In the present study, male preponderance was common with 66% as mentioned in many other studies, which may be due to greater risk of hypertension, life style modification and increased incidence of smoking & Alcoholism as risk factors. But our study differs with few international studies mentioning female dominance in cases of stroke which may be difference in the study group involved and age related hormonal changes and associated systemic diseases.⁵ The incidence of diabetics in the study was 36% and all were of Type 2 Diabetics. Male preponderance was observed in our study among the diabetics which is similar to many studies with the range of 35-64% universally. The accumulation of traditional risk factors and

along with aging in males is likely to explain the male predominance among patients of our study. However the difference in gender proportion was not statistically significant in our study. The most common age group in our study was 60-69 years which is similar to many studies in India and few studies have mentioned the incidence of stroke was common in age group of 40-50 years which may be due to association of risk factors at an early age and association of modifiable risk factors at an early age. As per study done by Ho JE *et al.* during the premenopausal years, women have fewer strokes than men but the incidence levels were off after 60 year.⁶ Among the diabetics in our study, major associated risk factor was hypertension followed by smoking. Finding of our study correlates with the finding of Kamalakannan S *et al.* who reported the association hypertension among diabetics in his study as high as 75%.⁷ In addition to these diabetes associated specific risk factors, also genetic, demographic and life style related factors also contribute in various degrees to the overall risk of subjects with diabetes mellitus. Although the association of dyslipidemia and ischemic stroke is not as clear as in coronary artery disease, evidence is compelling that increased stroke risk is associated with high levels of total cholesterol, and low high-density lipoprotein levels. In our study also results shown that high levels of total cholesterol and low-density lipoprotein, and low high-density lipoprotein levels association with ischemic stroke. Findings of our study correlate with the findings of Mary Grace *et al.* in their study.⁸

In the present study, a clear statistical significant association was observed between levels of Hb1Ac and the severity of the stroke. Majority of the patients with Hb1Ac levels >6.5 were presented with NIHSS score (13-16) and <6.5 presented with NIHSS score (8-12). 56 cases with Hb1Ac >6.5 were in Group 3 and 99 cases with Hb1Ac <6.5 were in Group 2. Thus, most patients with a better prognosis as determined by their lower NIHSS score had a lower HbA1c level, and most with a worse prognosis as per their higher NIHSS score had a higher HbA1c level. Findings of our study correlated well with the findings of Patibandla S *et al.*⁹

In our study, 38.34% of the cases were placed in Group 2 with NIHSS score 8-12. This finding correlated with the finding of Sarkar RN *et al.* who reported 42% of his cases were in Group 2.¹⁰ Majority of the diabetics during admission were placed in the Group 3 with NIHSS score of 13-16 (65/108) which is on par with the finding of O'Neill PA with 48% in his study.¹¹ In our study ischemic stroke patients with Diabetes mellitus have a significantly increased risk for stroke compared with non diabetic patients and the severity of the stroke was moderate when compared with non diabetic patients. Our finding contrasts with the findings of Kaarisalo MM *et al.* who observed diabetes has no significant association with stroke severity in his study.¹²

Diabetic ischemic stroke patients have worse prognosis up to one month follow up period compared with non diabetic patients, which was proven in other studies. In our study diabetics have no statistically significant worsening effect in prognosis of ischemic stroke patients after one month follow up period compared with non diabetic patients. These findings were similar to the findings of many studies globally but contrast to the finding of Kizer JR *et al.*¹³ our study clearly emphasizes that there was a statistically significant difference in the prognosis of non diabetics than diabetics. In the present study, the percentage of mortality at the end of three months follow up was 5.3%. The incidence of mortality was significantly higher in diabetics than non diabetics which is similar to the findings in the study of Tuttolomondo A *et al.*¹⁴ However our study findings were in contrast to the findings of Megherbi SE who mentioned no association between diabetes and severity of stroke and mortality, but with a significant association between dyslipidemia and outcome of stroke in his study.¹⁵

To conclude, our study found a significant association between diabetes and severity of stroke with NIHSS scoring as a tool of predictor in severity. A significantly higher blood glucose levels and Hb1Ac result in higher mortality and poorer outcomes. The limitation of our study was less number of sample populations to represent a large scale Indian population. The low number of follow up cases will not be able to make up a significant association of diabetes and AIS. Based on the observations on our study, diabetes increased the risk of severity of stroke and dependent outcome among the acute ischemic stroke patients.

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Conflict of Interest: NIL.

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