

## Role of HbA1c at Admission on Severity and Functional Outcome of Ischemic Stroke in Patients with Diabetes Mellitus

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### Abstract

**Background:** Diabetes mellitus the metabolic disorder can interact with atherosclerosis in ischemic strokes to initiate activate and propagate vascular events. To formulate effective preventive measures, it is mandatory to understand the impact of the glycemic status on the severity and functional outcome of Acute Ischemic stroke in patients with diabetes.

**Purpose of the study:** Study the effect of Glycemic status at admission on severity and outcome of Acute Ischemic stroke in patients with diabetes.

**Materials and methods:** The study is a prospective, case-control, hospital based study done at Department of Neurology, Narayana medical college for a period of 1½ year.

**Results:** 130 acute ischemic stroke patients were studied. 100 patients were cases with diabetes mellitus. Remaining 30 patients were controls without diabetes. Case were subcategorised to good glycemic control (HbA1c<7) and poor glycemic control (HbA1c>7) 97.5% patients of poor glycemic control group has moderate to severe stroke severity >7 (NIHSS) at admission and 53.3% of good glycemic control patients has mild severity (NIHSS=1-6). 95% of good glycemic control group and 96.7% of non-diabetic control group patients have functional independence at 3 months of follow up. 47.5% of Poor glycemic control patients have functional dependence at 3 months of follow up.

**Conclusion:** Glycemic control has significant association on severity and outcome of ischemic stroke patients with diabetes. 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 and diabetes mellitus.

**Keywords:** HbA1c; Severity; Outcome; Ischemic stroke; Diabetes

### Introduction

Stroke is the most common clinical manifestation of cerebrovascular disease which represents one of the clinical endpoint of atherosclerosis. It is the disease of the cerebral blood vessels nourishing the brain. World Health Organisation (WHO) defines stroke as an event caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. Stroke is a global health problem. It is the second commonest cause of death and fourth leading cause of disability worldwide [1].

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. Diabetes mellitus is a very common metabolic disorder with high and increasing prevalence worldwide.

Risk factors for macrovascular disease in diabetic individuals include dyslipidemia, hypertension, obesity, reduced physical activity, and cigarette smoking. Additional risk factors more prevalent in the

diabetic population include microalbuminuria, an elevation of serum creatinine, and abnormal platelet function. Glycemic status is an important variable that can affect the severity and outcome of stroke in patients with diabetes mellitus.

Few studies in literature had revealed the importance of fasting blood glucose [2-6], fasting insulin levels and HbA1c levels on the stroke severity and outcome. In our present study we compared the glycemic status and other risk factors in relation to stroke severity and the functional outcome after a period of 3 months in southern Indian diabetic and non-diabetic population.

### Aims and Objectives

To know the glycemic status by estimating the HbA1c, Fasting and Postprandial plasma glucose at admission among patients with acute ischemic stroke. To study the effect of HbA1c on the severity of stroke at admission and functional outcome at the end of 3 months in acute ischemic stroke patients with diabetes and without diabetes. To compare the poor and good glycemic status patients among the diabetics for the competence of glycemic status on the severity and functional outcome of stroke.

The efficacy of glycemic status especially HbA1c in predicting the severity and functional outcome of acute ischemic stroke can be further emphasized, by comparing it among the poor and good glycemic diabetics with the non-diabetic group patients

## Materials and Methods

The present study was done at department of neurology, Narayana medical college, Nellore for a period of 1 and ½ year from January 2014 to June 2015. The current study was a prospective case-control, hospital based study and was approved by the institute ethical committee of Narayana medical college and hospital. The study was done on the patients of Endocrinology, Neurology OPDs and Emergency departments.

A total of 100 acute ischemic stroke patients with diabetes as cases. Cases (All acute ischemic stroke patients with diabetics) were categorised into 2 sub-groups based HbA1c level at the time of admission as acute ischemic stroke patients with diabetes with good glycemic control (<7 HbA1c) and acute ischemic stroke patients with diabetes with poor glycemic control (>7 HbA1c). 30 acute Ischemic stroke patients without diabetes as controls. Patients were included in the study after a detailed informed consent.

### Inclusion criteria

- Acute Ischemic stroke patients

### Exclusion criteria

- Intra cerebral haemorrhage

- Space occupying lesions
- Sub arachnoid haemorrhage
- Cerebral venous thrombosis
- Transient ischemic attacks
- Patients with recurrent cerebrovascular events

A Proforma was prepared which includes detailed history, clinical examination and requisite investigations available at Narayana hospital. History includes all of the symptoms pertaining to the ischemic stroke in detail with emphasis on all the risk factors including the glycemic status at the time of admission.

Glycemic status in acute ischemic stroke patients with diabetes was evaluated by measuring the HbA1c level and fasting and post prandial plasma glucose levels. The stroke severity at admission was assessed based on NIHSS and patients were followed up to discharge and 3 months subsequently. The stroke functional outcome at 3 months was assessed by mRS.

## Statistical Analysis

The data values have been entered into MS-Excel and statistical analysis had been done by using IBM SPSS Version 20.0. For categorical variables the values were represented as number and percentages. To test association between the groups, chi-square test had been used. For continuous variables, the values were represented as mean and standard deviation. To test the mean difference between three or more groups, ANOVA (Analysis of Variance) test with post hoc (Tukey's) test had been used. All the p values were having less than 0.05 were considered as statistically significant.

CATEGORICAL VARIABLES								
S No.	Variable	GGC N (%)	PGC N (%)	Non-Diabetic N (%)	Total N (%)	Chi-Square	P-Value	
1	Sex	F	20 (33.3)	8 (20.0)	8 (26.7)	36 (27.7)	2.151	0.341
		M	40 (66.7)	32 (80.0)	22 (73.3)	94 (72.3)		
2	Smoking	No	42 (70)	16 (40)	20 (66.7)	78 (60)	9.722	*0.008
		Yes	18 (30)	24 (60)	10 (33.3)	52 (40)		
3	Alcohol	No	48 (80)	21 (52.5)	20 (66.7)	89 (68.5)	8.464	*0.015
		Yes	12 (20)	19 (47.5)	10 (33.3)	41 (31.5)		
4	HTN	No	23 (38.3)	9 (22.5)	14 (46.7)	46 (35.4)	4.803	0.091
		Yes	37 (61.7)	31 (77.5)	16 (53.3)	84 (64.6)		
5	Carotid/Vertebral Doppler	No	55 (91.7)	29 (72.5)	30 (100)	114 (87.7)	13.643	*0.001
		Yes	5 (8.3)	11 (27.5)	0 (0)	16 (12.3)		
6	Toast	Cardio Embolic	2 (3.3)	1 (2.5)	0 (0)	3 (2.3)	0.995	0.608
		Large Artery	58 (96.7)	39 (97.5)	30 (100)	127 (97.7)		

**Table 1:** Baseline descriptive statistics for good glycemic control (GGC), poor glycemic control (PGC) and control group (non-diabetics) [TOAST: Trial of ORG 10172 in Acute Stroke Treatment; HTN: Hypertension].

## Results

Total number of patients analysed for the study: 130, cases were 100 acute ischemic stroke patients with diabetes. They were grouped into good glycemic control <7 HbA1c (No=60), poor glycemic control >HbA1c (No=40). Controls were 30, (acute ischemic stroke patients without Diabetes).

Males were predominant (94/130) comprising 72.3% of study population. Mean age of patients was  $56.78 \pm 12.925$  years. Non-smokers (60%) were more when compared to smokers (40%). Most of the patients were non-alcoholics (68.5%). Hypertension was noted in 64.6% of patients (Table 1).

Significant hemodynamic changes (>50% stenosis and flow dynamics) were noted in 16 patients (12.3 %) out of 130 acute ischemic stroke patients. Out of 16, 11 patients were poor glycemic control group and 5 from good glycemic control. None of the non-diabetic patients had significant doppler findings. Based on TOAST classification for etiology, 127 patients had large artery to artery atherosclerotic etiology, whereas, 3 patients had cardio-embolic etiology.

For the patients distribution among these sub groups age, smoking, alcoholism had significant correlation ( $p < 0.05$ ). Sex and hypertension did not have positive correlation among patients of 3 groups. Significant hemodynamic abnormalities on carotid/vertebral doppler were mostly noted in poor glycemic control patients when compared to good glycemic control and non-diabetic subgroup patients with  $P = 0.001$ . TOAST classification for etiology had no significant statistical distribution among 3 groups of patients. 60% of patients of poor glycemic control were smokers whereas nearly 65% of patients of good glycemic control and non-diabetic group were non-smokers. Similarly majority of alcoholic patients were from poor glycemic control group.

Patients of poor glycemic control had high total cholesterol, VLDL, TGL values when compared to good glycemic control and non-diabetic groups ( $P < 0.05$ ) (Table 2) Despite high mean LDL values noted in poor glycemic control patients, it had no statistically significant correlation. High mean HDL values were noted in good glycemic control patients and it had no statistical correlation among three groups. TGL/HDL had also statistical significance (0.003) distribution among 3 groups.

CONTINUOUS VARIABLES							
S No.	VARIABLE	GGC	PGC	NON-DIABETIC	TOTAL	F-VALUE	P-VALUE
		NO:60	NO:40	NO:30	130		
1	AGE	53.53 ± 11.864	59.95 ± 12.397	59.03 ± 14.459	56.78 ± 12.925	3.7	* 0.027
2	TOTAL (CHOL)	186.78 ± 39.266	207.63 ± 47.669	173.23 ± 48.680	190.07 ± 45.732	5.493	* 0.005
3	HDL	46.02 ± 11.425	45.35 ± 14.677	44.67 ± 13.311	45.5 ± 12.843	0.133	0.893
4	LDL	104.15 ± 31.418	113.08 ± 42.340	102.87 ± 34.859	106.6 ± 35.856	0.954	0.388
5	VLDL	30.40 ± 14.141	42.6 ± 20.808	22.03 ± 8.888	32.22 ± 17.297	15.625	* < 0.0001
6	TGL	141.12 ± 55.986	181.50 ± 76.827	112.73 ± 44.058	146.99 ± 65.671	11.438	* < 0.0001
7	TGL/HDL	3.2922 ± 1.68654	4.8901 ± 4.52607	2.6880 ± 1.07635	3.6444 ± 2.91654	6.154	* 0.003
8	FPG	103.80 ± 24.534	161.28 ± 55.449	97 ± 22.148	119.92 ± 45.7	37.34	* < 0.0001
9	PPG	133.47 ± 37.989	209.53 ± 65.216	120.33 ± 27.977	153.84 ± 59.477	42.366	* < 0.0001
10	HbA1C (ADM)	5.9217 ± 0.46106	8.5050 ± 1.26003	5.74 ± 0.40224	6.6746 ± 1.45577	155.823	* < 0.0001
11	TSH	5.4572 ± 4.031718	4.6955 ± 2.41902	2.2783 ± 1.23521	4.4892 ± 3.49602	9.467	* < 0.0001
12	NIHSS(ADM)	6.47 ± 2.213	12.3 ± 3.180	8.73 ± 4.315	8.78 ± 3.977	42.401	* < 0.0001
13	mRS(3M)	1.15 ± 0.732	2.23 ± 1.050	1.53 ± 0.730	1.57 ± 0.956	19.584	* < 0.0001

**Table 2:** Baseline descriptive statistics for good glycemic control (GGC), poor glycemic control (PGC) and control group (non-diabetics). [Chol: Cholesterol; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; VLDL: Very Low Density lipoprotein; TGL: Triglycerides; FPG: Fasting Plasma Glucose; PPG: Post prandial Plasma Glucose; TSH: Thyroid Stimulating Hormone; NIHSS: National Institute of Health Stroke Score; mRS: modified Rankin Score; HbA1c: Glycated Haemoglobin; ADM: Admission].

Glycemic status indicators like FPG, PPG, HbA1C had very high statistical significance (0.0001) values among 3 groups of patients. High mean FPG of 161.28 mg/dl was noted in poor glycemic control groups when compared to 103.8 mg/dl in good glycemic control 97 mg % in non-diabetic group. PPG also had similar trend of statistical distribution among 3 groups with high mean PPG of 209.53 mg% was noted in poor glycemic group. Poor glycemic control group had

statistically significant high HbA1c value  $8.5 \pm 1.26$  when compared to good glycemic control group ( $5.92 \pm 0.46$ ) and non-diabetics ( $5.74 \pm 0.4$ ).

TSH values were significantly high among diabetic (good and poor glycemic) group compared to control group (<0.0001).

**Stroke severity at admission (NIHSS) in cases vs. control groups**

patients (53.3%) of good glyceic control had mild severity (NIHSS=1-6) (Table 3).

97.5% patients of poor glyceic control group had moderate to severe stroke severity (>7 NIHSS) at admission. Whereas half of

S No.	NIHSS	Variable	GGC N (%)	PGC N (%)	Non-diabetic N (%)	Total N (%)	Chi-Square	P-Value
1	Mild	6-Jan	32 (53.3)	1 (2.5)	10 (33.3)	43 (33.1)	55.259	* <0.0001
	Moderate	12-Jul	27 (45)	20 (50)	19 (63.3)	66 (50.8)		
	Severe	>12	1 (1.7)	19 (47.5)	1 (3.3)	21 (16.2)		

**Table 3:** Stroke severity at admission (NIHSS) in cases vs. control groups.

**Stroke functional outcome at 3 months (mRS) in cases vs. control groups**

poor glyceic control patients had functional dependence at 3 months of stroke follow up. Statistics significantly illustrates glyceic effect on functional outcome of acute ischemic stroke patients at 3 months follow up (Table 4).

Significant percentage of good glyceic control group (95%) and non-diabetic control group (96.7%) patients had functional independence at 3 months of stroke follow up. Proportionally 47.5% of

S. No	mRS	Variable	GGC N (%)	PGC N (%)	Non-diabetic N (%)	Total N (%)	Chi-Square	P-Value
1	Independent	0-2	57 (95)	21 (52.5)	29 (96.7)	107 (82.3)	35.291	* <0.0001
	Dependent	6-Mar	3 (5)	19 (47.5)	1 (3.3)	23 (17.7)		

**Table 4:** Stroke functional outcome at 3 months (mRS) in cases vs. control groups.

S. NO	Variable	GGC		PGC		P value
		NO: 60		NO: 40		
1	Age	53.53 ± 11.864		59.95 ± 12.397		* 0.038
2	Total (Chol)	186.78 ± 39.266		207.63 ± 47.669		0.058
3	HDL	46.02 ± 11.425		45.35 ± 14.677		0.965
4	LDL	104.15 ± 31.418		113.08 ± 42.340		0.444
5	VLDL	30.40 ± 14.141		42.6 ± 20.808		* 0.001
6	TGL	141.12 ± 55.986		181.50 ± 76.827		* 0.004
7	TGL/HDL	3.2922 ± 1.68654		4.8901 ± 4.52607		* 0.017
8	FPG	103.80 ± 24.534		161.28 ± 55.449		* <0.0001
9	PPG	133.47 ± 37.989		209.53 ± 65.216		* <0.0001
10	HbA1C (ADM)	5.9217 ± 0.46106		8.5050 ± 1.26003		* <0.0001
11	TSH	5.4572 ± 4.031718		4.6955 ± 2.41902		0.494
12	NIHSS (ADM)	6.47 ± 2.213		12.3 ± 3.180		* <0.0001
13	mRS (3M)	1.15 ± 0.732		2.23 ± 1.050		* <0.0001

**Table 5:** Baseline descriptive statistics for good glyceic control (GGC) and poor glyceic control (PGC) groups.

**Good glyceic control vs. poor glyceic control**

Dyslipidemic fractions like VLDL, TGL, TGL/HDL and glyceic indicators like FPG, PPG and HbA1c were having positive statistical

correlation between the two groups. Poor glyceic control group had high stroke severity at admission and dependant functional outcome at 3 months when compared to good glyceic control group patients.

Glycemic control had significant association on severity and outcome of ischemic stroke patients with diabetes (Table 5).

### Poor glycemic control vs. non-diabetics

There were statistically significant correlations noted between the poor glycemic control group and non-diabetic group. Poor glycemic control group had high stroke severity at admission and dependant functional outcome at 3 months when compared to control group patients (Table 6).

S No.	Variable	PGC	Non-Diabetic	p-value
		NO:40	NO:30	
1	Age	59.95 ± 12.397	59.03 ± 14.459	0.952
2	Total (Chol)	207.63 ± 47.669	173.23 ± 48.680	* 0.005
3	HDL	45.35 ± 14.677	44.67 ± 13.311	0.974
4	LDL	113.08 ± 42.340	102.87 ± 34.859	0.468
5	VLDL	42.6 ± 20.808	22.03 ± 8.888	* <0.0001
6	TGL	181.50 ± 76.827	112.73 ± 44.058	* <0.0001
7	TGL/HDL	4.8901 ± 4.52607	2.6880 ± 1.07635	* 0.004
8	FPG	161.28 ± 55.449	97 ± 22.148	* <0.0001
9	PPG	209.53 ± 65.216	120.33 ± 27.977	* <0.0001
10	HbA1C (ADM)	8.5050 ± 1.26003	5.74 ± 0.40224	* <0.0001
11	TSH	4.6955 ± 2.41902	2.2783 ± 1.23521	* 0.008
12	NIHSS (ADM)	12.3 ± 3.180	8.73 ± 4.315	* <0.0001
13	mRS (3M)	2.23 ± 1.050	1.53 ± 0.730	* 0.003

**Table 6:** Baseline descriptive statistics for poor glycemic control (PGC) and Non diabetics.

### Good glycemic control (GGC) and non-diabetics

There were no statistical significant associations between the two groups regarding age and dyslipidemic fractions except for VLDL. Similarly glycemic indicators (FPG PPG and HbA1c) were not different between the groups. Interesting finding to be noted was stroke severity and functional outcomes are not different between the ischemic patients of good glycemic control group and non-diabetic group. TSH was significantly higher among diabetic patients compared to non-diabetics but it was not significantly different between good and poor glycemic control groups (Table 7).

S No.	Variable	GGC	Non-Diabetic	p value
		NO: 60	NO: 30	
1	Age	53.53 ± 11.864	59.03 ± 14.459	0.131
2	Total (Chol)	186.78 ± 39.266	173.23 ± 48.680	0.359
3	HDL	46.02 ± 11.425	44.67 ± 13.311	0.887
4	LDL	104.15 ± 31.418	102.87 ± 34.859	0.986
5	VLDL	30.40 ± 14.141	22.03 ± 8.888	*0.047

6	TGL	141.12 ± 55.986	112.73 ± 44.058	0.097
7	TGL/HDL	3.2922 ± 1.68654	2.6880 ± 1.07635	0.602
8	FPG	103.80 ± 24.534	97 ± 22.148	0.684
9	PPG	133.47 ± 37.989	120.33 ± 27.977	0.417
10	HbA1C (ADM)	5.9217 ± 0.46106	5.74 ± 0.40224	0.56
11	TSH	5.4572 ± 4.031718	2.2783 ± 1.23521	* <0.0001
12	NIHSS(ADM)	6.47 ± 2.213	8.73 ± 4.315	0.064
13	mRS(3M)	1.15 ± 0.732	1.53 ± 0.730	0.108

**Table 7:** Baseline descriptive statistics for good glycemic control (GGC) and non-diabetics.

### Discussion

Ischemic stroke is a heterogeneous pathophysiological state in which varied different pathways might lead to indistinguishable clinical presentations that result in high mortality rates and severe disabilities. Well recognized etiologies of ischemic stroke include cardiac or artery-to-artery embolism and atherothrombosis of an extracranial and intracranial carotid and vertebral artery systems due to Type 2 diabetes mellitus. However, it is generally accepted that atherosclerosis of extracranial or intracranial arteries due to Type 2 diabetes mellitus accounts for a substantial proportion of clinical ischemic strokes.

This is one of few clinical studies where the role of glycemic status is systematically evaluated with respect to stroke severity and functional outcome.

The current study reports a prospective study which includes 130 patients recruited from emergency and outpatient departments of Neurology who were admitted with acute ischemic stroke. As in other studies [7,8], the current study also showed male predominance. The accumulation of traditional risk factors and along with aging in males is likely to explain the male predominance among acute ischemic stroke patients.

The current study shown that smoking had statistical distribution among all the three groups of patients. Majority of poor glycemic control group patients were smokers when compared to non-diabetic group, similar finding was noted by other studies [9-11]. There is significant evidence that smoking increases the risk of diabetes. Smoking is associated with central obesity. Smoking also increases inflammation and oxidative stress, to directly damage β-cell function and to impair endothelial function.

Alcohol also had similar association with diabetes among three groups where predominant alcoholics were from poor glycemic control which is consistent with other series reported by some authors [12-14].

Diabetes mellitus is recognized clinically as a complication of alcoholism. Heavy amounts of alcohol show direct diabetogenic effects with its contribution to excess caloric intake and obesity, induction of pancreatitis, disturbance of the carbohydrate and glucose metabolism and the impairment of the liver function, which affects the blood glucose levels.

TSH was significantly higher among diabetic patients compared non-diabetic but it was not significantly different between good and poor glycemic control groups.

The prevalence of thyroid disorder in diabetic population was reported to be 13.4% with higher prevalence (31.4%) in female type 2 diabetic patients as compared to (6.9%) in male type 2 diabetic patients [15]. The prevalence of thyroid dysfunction in type 2 diabetic patients was reported to be 12.3% in Greece and 16% in Saudi Arabia by Akbar et al. [16] considerably; type 2 diabetic patients were more prone to thyroid disorders. The prevalence of thyroid disorders was as high as 31% in a study done from India [17].

The pathophysiological pathway connecting these two disorders has not been clearly delineated as of now. The most obvious connection, perhaps, is the increased BMI and insulin resistance common to both conditions. Obesity, stroke is associated with an altered milieu with increase in proinflammatory markers and increase in insulin resistance. This, through undefined mechanisms, leads to decreased deiodinase2 activity at pituitary level resulting in relative T3 deficiency and increase in TSH levels [18]. The exact mechanism by which poor glycemic control affects severity and outcome of ischemic stroke patients is less clear. General complications related to poorly controlled glycemic status could be one explanation. An increased HbA1C level reflects poor long term glycemic control and has its specific implications on the structure and function of vascular bed including small as large cerebral vessels. Increased HbA1c level might also be a marker of poor compliance indicating an unhealthy life style.

Evidence is compelling that increased stroke risk is associated with high levels of total cholesterol and low-density lipoprotein, and decreased high-density lipoprotein levels. In the Helsinki young stroke registry [19], dyslipidemia was clearly the most prominent well documented risk factor. In the present study also results shown that high mean levels of total cholesterol (<0.005) and very low-density lipoprotein (<0.0001), and Triglycerides (<0.0001) levels in patients of ischemic stroke with poor glycemic control when compared with good glycemic control and Non-diabetics ischemic stroke patients [20-22].

Kizer et al. [23] studied the relationship between HbA1c and stroke. The results showed that after adjusting age, gender, smoking, blood lipids and other variances, HbA1c and stroke risk was significantly associated. They emphasized that strict control of glycated haemoglobin (HbA1c) might be benefit for stroke prevention for the patients with diabetes. The present study showed that FPG, PPG values on admission, NIHSS scores, three months MRS score, when compared among three groups of patients, the difference was statistically significant ( $P < 0.0001$ ). Patients with high HbA1c, high FPG, high PPG had high NIHSS score at admission with poor outcomes at 3 months ( $P < 0.001$ ). That is to say, a higher HbA1c level will have a more serious neurological impairment, and the clinical condition might be more serious. So, HbA1c levels at admission might be an important predictor to evaluate the neurological impairment in patients with acute ischemic stroke. In neurological impairment aspect, on admission, serious patients (>12 NIHSS) of poor glycemic control accounted for 47.5%, that is higher than good glycemic control (1.7%) and non-diabetics (3.3%). In three months functional outcome aspects, dependent (>2 MRS) patients of poor glycemic control group accounted for 47.5%, that is higher than good glycemic control (5%), non-diabetic (3.3%). And a higher HbA1c levels has a more serious neurological impairment on admission and the prognosis is worse after three months. The mechanism might be associated with long-term high blood glucose and high blood HbA1c, which lead to lesions of

large blood vessels and which lead to oxygen dissociation curve to the left, resulting in oxygen dissociation barrier, nerve tissue ischemia and hypoxia, that is not benefit for the recovery of neurological function, and the prognosis is worse. This result is in line with the result of Kamouchi et al. [24], who studied 3627 patients, the result showed that neurological improvement is lower relevant to age and sex and is higher relevant to the blood HbA1c level on admission. In summary, the current study suggests that blood HbA1c levels on admission may influence severity in patients with acute ischemic stroke and may adversely predict three months prognosis. So, HbA1c levels maybe is an important predictors to evaluate the neurological impairment and three months prognosis in patients of acute ischemic stroke with diabetes.

Therefore, effectively lowering blood HbA1c levels may reduce the severity of neurological impairment in patients with acute ischemic stroke, and may be can improve the life quality of patients with acute ischemic stroke.

A novel and very unique finding we derived from our study is that maintaining good glycemic goal is equally effective in reducing stroke severity and improved functional independence at 3 months of follow up when compared with Non-diabetic status. This conclusion is evident by no statistical correlation between the groups with reference to stroke severity (<0.06), stroke functional outcome (0.108).

Limitation of this study is that we did not measure the size of the stroke lesion by CT or MRI, however it is well known that NIHSS score is a good clinical severity measure, which parallels infarct volume. We have not considered diabetic complications and other complications related to other systems during follow up period which will affect the prognosis.

Based on results from this prospective study additional studies are needed to elucidate desired glycemic goal (HbA1C less than 7) for prevention of ischemic stroke and to effectively decrease stroke severity and improve functional outcome of acute ischemic stroke.

Further studies are needed to elucidate whether treatment to provide good glycemic control before onset of stroke improves clinical course and outcome in patients with ischemic stroke.

## Conclusion

By performing the study with non-diabetic controls the current study was able to analyse and identify distinctly the clinical effects of diabetes mellitus on the outcome of acute ischemic stroke. Among the diabetic stroke patients the severity of deranged glycemic status found to have an influencing effect on the stroke severity and functional outcome. 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. 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.

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