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Prognostication of Ischemic Stroke Outcome Based on the Glycemic Control

KEYWORDS: Diabetes mellitus, Stroke, hyperglycemia, normoglycemia

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ABSTRACT *Diabetes mellitus is a well-recognized risk factor for stroke. Stroke in hyperglycemics is different from stroke in normoglycemic patients from several perspectives.*

Aims:
To compare distinctive patterns between hyperglycaemic and normoglycemic stroke, and to correlate the effect of admission glucose levels on the outcome of both groups.
Settings and Design:
The present study is prospective case control observational study, carried out at two Hospitals in South Delhi. All cases having acute onset ischemic stroke between Apr 2011 and Apr 2013 and meeting strict inclusion and exclusion criteria were included in the study. Acute stroke was confirmed by physical examination and CT brain to have ischemic stroke.
Research question- whether patients of acute ischemic stroke presenting with hyperglycemia at onset will have a different functional outcome as compared to patients with normo-glycemia at the end of 3 months?
Results: Fifty patients with ischemic stroke were enrolled (Thirty were hyperglycemics or found to have hyperglycemia at time of admission / at onset of stroke and twenty were normoglycemic patients). Mean admission blood sugar was higher in hyperglycemics than normoglycemic group. Admission hyperglycemia or diabetic patients have worse outcome in the form of more severe disability and dependency at 90 days from the onset of stroke as compare to normoglycemic patients.
Conclusions:
Stroke in hyperglycemic patients has poor prognosis which emphasizes the need for early diagnosis and treatment of diabetes. Admission hyperglycemia / hyperglycemia at onset of stroke in diabetic patients has severe stroke with the worse outcome on day 90 from onset of ischemic stroke as compared to normoglycemic patients. Knowledge gap is that the relationship between stroke outcome and blood sugar has not been studied on Indian population in the past.

Introduction:
World Health Organisation defines the clinical syndrome of "Stroke" as rapidly developing clinical signs of focal (or global) disturbance of cerebral function with symptoms lasting 24 hrs or longer or leading to death with no apparent cause other than vascular origin.[1] Modifiable risk factors for stroke include hypertension, diabetes mellitus, hyperlipidaemia, cigarette smoking, cardiac disease, drug abuse, heavy alcohol consumption, and AIDS.[2] DM is a modifiable risk factor for a first ischaemic stroke.[3] In people with diabetes mellitus, there is increased risk for stroke compared with those without diabetes.[2,3] Modifiable risk factors for stroke include hypertension, diabetes mellitus, hyperlipidemia, cigarette smoking, cardiac disease, drug abuse, heavy alcohol consumption, and AIDS.[4] Ischemic stroke is often thought to be a single entity, but in fact it may be the result of quite different disease processes.[5]

Diabetes poses a major health problem and is one of the top five leading causes of death in most developed countries. The previous evidence suggests that it could reach epidemic proportions particularly in developing and in newly industrialized countries.[6] 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.[7, 8]

The incidence of stroke also increases with increasing age, thus many stroke patients may have undetected diabetes at the time of stroke; subsequent examination in 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 difference in ascertainment. Diabetes potentiates stroke by favouring thrombosis by increasing concentration in blood of post thrombotic factors like fibrinogen and von Wiillebrand factor. It also increases platelet adhesiveness. Fibrinolytic capacity is decreased through increased concentrations of plasminogen activator inhibitor type1. Diabetes also favours atherogenesis because of various lipid abnormalities like hypertriglyceridemia, low HDL and high triglyceride en-riched HDL. Glycosylation of lipoproteins and oxidation of lipoproteins leads to atheroma formation.[9] The effect of hyperglycemia on mortality is large.[10]

McCall has noted that a higher blood glucose level at hospital admission predicts a poorer prognosis after a stroke, irrespective of whether the patient is diabetic or not. Also, the degree of disability after stroke may be worse among individuals with elevated blood glucose at time of stroke. Animal models showed that hyperglycaemia alone worsens the ischemic brain damage from a stroke. [11]

Wier et al. also showed that raised plasma glucose levels after acute stroke predicts a poorer prognosis after correcting for age, stroke severity, and stroke subtype. Raised

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plasma glucose concentration is therefore unlikely to be solely a stress response and should arguably be treated actively. 12

Subjects and Methods:
The study was carried out on 50 patients presenting with acute ischemic stroke in two hospitals of South Delhi. All cases having acute onset ischemic stroke between Apr 2011 and Apr 2013 and meeting strict inclusion and exclusion criteria were included in the study. Acute stroke was confirmed by physical examination and CT brain to have ischemic stroke.

Research question- whether patients of acute ischemic stroke presenting with hyperglycemia at onset will have a different functional outcome as compared to patients with normo-glycemia at the end of 3 months?

The inclusion criteria- Age 18years or older, Clinical diagnosis of ischemic stroke with acute neurological deficit of less than 24hrs duration, and must arrive at hospital within 48hrs of symptom onset. Patients must have an NIH Stroke Scale Score of 4 to23.

The exclusion criteria -Age below 18 years., renal dysfunction (serum creatinine >/= 2.5), pre-existing psychiatric illness that would be confound neurological assessment, pregnant patients, patients with life threatening conditions that makes them unlikely to survive 90 days / Patients who are unable to come back for 90 day fallow up, and patients who are unwilling or unable to give informed consent. A random blood sugar value of 180mg/dl or more is considered as hyperglycemia and normoglycemia being random blood sugar<130 mg/dl. Blood sugar was monitored in first 48hrs and subsequently at 7 days and at 90 days. After admission detailed history regarding temporal profile of stroke and risk factors like, diabetes, smoking, alcohol intake, and previous strokes were documented. Detailed neurological examination was done and stroke score based on NIHSS was recorded at admission. Outcome of these patients was assessed on the basis of disability and dependency using modified Rankin scale (MRS) and Barthel Index respectively at the end of 3 months in relation to the glycemic status at the time of onset of stroke.

Results:
This study includes a total of fifty subjects with clinical and radiological diagnosis of ischemic stroke. They are divided into two groups; group one with hyperglycemia and group two with normoglycemia, on the basis of random blood sugar (RBS) at onset of stroke, more than 180 mg% and less than 130 mg% respectively. Group one contains 27 and groups two contains 23 patients. Patients in both the groups presented with motor weakness as their most common presenting complaint (90% in both the groups had hemiplegia/hemiparesis and 8% had monoparesis / monoplegia.

The mean age in hyperglycemic patient was 58.0 ±9.8 years and in normoglycemics 60.5 ± 12.5 years, and the difference in the mean age in the study was not statistically significant. Out of twenty-seven patients with hyperglycemia nineteen were males and eight were females, where as in normoglycemics out of twenty-three patients, fifteen were males and eight were females. Among hyperglycemic patients 86% were known diabetics whereas 14% were newly detected diabetes. 68% of hyperglycemic patients had past history of hypertension compared to 32% in normoglycemic group which was statistically significant. Previous history of IHD was present in 26% of hyperglycemics and 6% of normoglycemic patients. Previous history of stroke was present in 30% of hyperglycemics and 15% of normoglycemic stroke patients. 5% of hyperglycemic and 42% of normoglycemic stroke patients had no history of addiction. History of tobacco chewing was 15% in hyperglycemics and 8% in normoglycemic patients. History of alcohol was in 18 % hyperglycemics and 26% in normoglycemic stroke patients. Incidence of smoking was 22% in hyperglycemics and 23% in normoglycemics.

The seventh cranial nerve was involved in about 26% of both the groups. Speech abnormality was present in 26% hyperglycemics and in 25 % normoglycemic patients. Other complications like headache and visual problem was present in about 9% hyperglycemics and 7% of normoglycemics.

The table 1 shows mean blood sugar on admission in hyperglycemic group was 231.81±81.50 mg% compared with 113.85±10.69 mg% in normoglycemic group. The difference was statistically significant (figure-1). The mean systolic blood pressure on admission was 142.5±22.7 mm Hg in hyperglycemics and 157.8 ±12.6 mm of Hg in normoglycemics. The mean diastolic blood pressure was on admission 82.2 ±13.2 mm of Hg in hyperglycemics and 96.3 ±7.1mm of Hg in normoglycemic group. The difference was statistically significant in both. The mean HDL was 33.10±9.65mg% in the hyperglycemic group and 40.65± 10.6mg% in normoglycemic group. The mean LDL was 105.63±40.50mg% in hyperglycemics and 120.40±43.10mg% in the normoglycemic group. The mean triglycerides were 188.6 ± 89.4mg% in hyperglycemics and 142.7 ±43.10mg% in normoglycemic group. Mean triglycerides was higher in the hyperglycemic group and mean HDL was lower in hyperglycemic group as compared to normoglycemic group. Both the values were statistically significant.

The severity of stroke at onset according to National Institute of health Stroke Scale (NIHSS) among the hyperglycaemic patients, 69% have severe stroke as compared to only 16% in normoglycemic group (figure-2 and 3). The difference was statistically significant.

Table 2 shows disability outcome at day 90 from onset of ischemic stroke in both groups according to modified Rankin scale (MRS) suggests that two patients died out of 27 in hyperglycaemic group and one died in normoglycemic group out to of 23 patients and hyperglycemic patients had severe disability. The outcome as compared to normoglycemic group at the end of 3 months. The difference was statistically significant

The dependency outcome at the end of 3 months from onset of ischemic stroke according to Barthel index. 24% patients had severe dependency in hyperglycaemic group as compared to 10 % in normoglycemic group. Only 8 % patients were independent in hyperglycemics as compared to 34% in normoglycemics at the end of 3 months. The difference was statistically significant.

Table -1. Blood glucose, blood pressure and cholesterol at admission

	Hyperglycemics	Normoglycemics	P-value

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	Mean	SD	Mean	SD	
Admission RBS (mg %)	231.81	81.50	113.85	10.69	P< 0.001, HS
SBP(mm of Hg)	142.5	22.7	157.8	12.6	P< 0.05, S
DSP(mm of Hg)	88.2	13.2	96.3	7.1	P< 0.05, S
HDL (mg %)	33.10	9.65	41.65	10.6	P< 0.05, S
LDL (mg %)	105.63	40.50	120.40	38.6	P< 0.05, NS
TG (mg)	188.6	89.4	142.7	43.10	P< 0.05, S

Table -2. Outcome at 90 days

	Hyperglycemics	Normoglycemics	P-value, S
Death	2 (7%)	1 (4%)	P>0.05,NS
No disability	3 (11%)	7 (48%)	P<0.05, S
Slight disability	8 (30%)	5 (22%)	P>0.05,NS
Severe disability	14 (52%)	10 (26%)	P<0.05, S

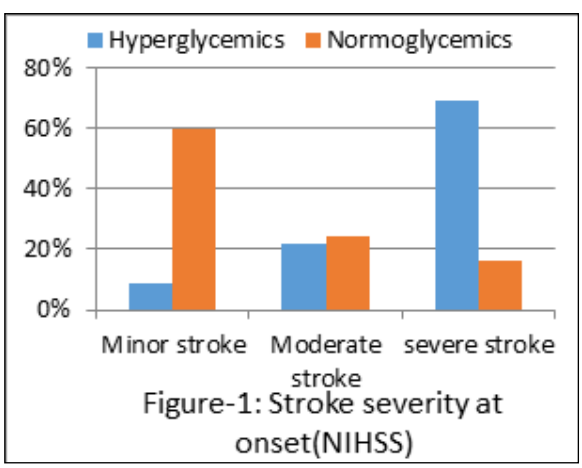

Figure-1: Stroke severity at onset(NIHSS)

Discussion:

Stroke is a very common clinical problem and with the current treatment available approximately 50% of patients are left with permanent disability with severe dependency. Effective risk factor intervention will be useful in reducing stroke morbidity and mortality. The observation in present study, that stroke occurs at younger age in hyperglycemics than in normolycemics was similar to other studies. The men were at greater risk for stroke in both hyperglycaemic and normoglycemic group was similar to above studies. Observation was contrary to that by Seppo Lehto et al 1996, who found that women are at greater risk for stroke than men. Also observation in the present study that past history of hypertension, ischemic heart disease and of stroke was more common in hyperglycemics than in normoglycemic group was similar to the above studies.

The observation in the present study that current or previous smoking was distributed equally between the two groups, but alcohol consumption was low in diabetic group was similar to the above study. The mean systolic and diastolic blood pressure was higher in normoglycemics than in hyperglycaemic group, was contrary to the above study. Hyperglycaemic patients were under treatment for hypertension unlike normoglycemics that could be the possible reason for low blood pressure on admission among hyperglycaemic patients. Also the observation in the present study that the admission random blood sugar (RBS) was higher in hyperglycemics then in normoglycemic group was similar to the above study.

In the present study, hyperglycaemic patients had higher mean triglycerides and lower HDL as compared to the normoglycemic group. Seppolehto et al (1996) observed hypertriglyceridemia and low HDL in hyperglycaemic stroke patients.[17] Kamel A et al (2006) found higher levels of triglycerides in hyperglycaemic as compared to normoglycemic group patients. [15]

In the present study, the stroke patients with hyperglycaemia had a poor outcome compared to normoglycemic patients. Similar observations were made by Megherbi SE [14] et al (2003), kamel A [15] et al (2006) and in Copenhagen Stroke Study (Jorgensen H [18] et al in 1994). Also in the present study, patients with hyperlycemia at stroke onset had more poorer out come as compared to those with lower blood sugar values in both hyperglycaemic and normoglycemic group. Similar observations were seen by McCall et al and Fuentes B [19] et al.

Conclusion:

Commonest modifiable risk factors in stroke are hypertension, smoking, dyslipidemia, alcohol consumption and diabetes mellitus. Diabetes is an independent risk factor for stroke. Stroke in diabetes differs from that of stroke in non-diabetics with respect to age, stroke type, stroke severity, prevalence of risk factors and outcome. Early diagnosis, treatment including life style modification and 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. Hyperglycemia at stroke onset is associated with higher risk of poor outcome independent of other variables. Treatment or prevention of modifiable risk factors can reduce the mortality and morbidity of stroke.

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