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Clinical Analysis of Ischemic Stroke in Patient with Diabetes Mellitus

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Abstract

Background and Aim: Diabetes mellitus by virtue of its association with micro vascular and macrovascular disease is an important risk factor in the genesis of stroke. Stroke is Twice more common in diabetics than in non diabetics**.** Objective of the present study was to measure the random blood glucose level in the early phase of ischemic stroke in both diabetics and in non diabetics and to evaluate the severity and prognosis in both diabetics and non diabetics in relation to hyperglycemia.

Material and Methods: Total of 120 of acute ischemic stroke patients admitted in the Institute of emergency medicine medical college & hospital were studied. Blood pressure measurement, blood sugar, urea, creatinine, electrolytes, hemoglobin, total count, differential count; urine sugar, albumin, deposits; electrocardiogram and chest X ray done for all patients. The severity of stroke for each patient is calculated based on NIH stroke scale. In patients with blood sugar more than 6.1 mmol/l (110 mg/dl) and without a history of diabetes, Hemoglobin A 1c was performed. The patients were followed up for thirty days and outcome in the form of death; poor, moderate and good improvements were recorded

Results: Among the 120 patients 64 had hypertension, 68 had diabetes, 58 had hypercholesterolemia, 6 had previous history of myocardial infarction and 2 female patients had atrial fibrillation. Hyperglycemic patients had a higher score when compared to Euglycemic patients, which was statistically significant. Among the admission day uncontrolled diabetes patients had the highest mean NIHSS. A positive correlation (r=0.71) between admission day

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sugar value and the outcome of stroke. Higher admission day elevated blood glucose level has increased mortality and high risk of poor functional recovery was seen in the results of the study.

Conclusion: There is a good correlation between admission day glucose level and the outcome in ischemic stroke. Admission day elevated glucose level was a significant predictor of mortality and poor functional outcome after acute stroke. Hence, restoration of normoglycemia as soon as possible should be encouraged.

Key Words: Blood Sugar, Diabetes mellitus, Hemoglobin, Stroke

Introduction

Stroke is one of the leading causes of death and long term disability in India. Stroke is an important cause of premature death and disability in low-income and middle-income countries like India, largely driven by demographic changes and enhanced by the increasing prevalence of the key modifiable risk factors.[1,2]

Among all the neurological diseases of adult life, a cerebrovacular accident clearly ranks first in frequency of importance. Almost fifty percent of neurological diseases in general hospital are due to stroke.[3,4]

Cerebro-vascular accident includes ischemic stroke, hemorrhagic stroke, and cerebro vascular anomalies such as intracranial aneurysm, AV malformation and cortical venous thrombosis. Stroke after heart disease, is the second most common cause of death among non-communicable diseases.[5]

With the introduction of effective treatment for hypertension, there has been a marked reduction in the frequency of stroke. Diabetes mellitus by virtue of its association with micro vascular and macrovascular disease is an important risk factor in the genesis of stroke. Most of the diabetic patients with stroke have raised glycosylated hemoglobin indicating that most of them have uncontrolled diabetes.[6,7]

Diabetics and stress hyperglycemics have severe strokes resulting in poor outcome. Stroke is Twice more common in diabetics than in non diabetics. Hypertension is common in diabetes and accelerates atherosclerosis which promotes intracranial small vessel disease and heart disease leading to lacunar and embolic infarction respectively. There are several risk factors that determine the outcome of stroke.[8-11]

Hyperglycemia, fever, neuroprotective agents are those which are widely studied. Hence the objective of the present study was to measure the random blood glucose level in the early phase of ischemic stroke (within 24 hours of onset) in both diabetics and in non diabetics and to evaluate the severity and prognosis in both diabetics and non diabetics in relation to hyperglycemia.

Material and Methods

Total of 120 of acute ischemic stroke patients admitted in the Institute of emergency medicine medical college & hospital were studied. The Patients were selected on the following basis

Inclusion Criteria

1. Patients should be above the age of forty

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2. Patients should have been admitted within twenty four hours of onset of symptoms
3. This should be the first cerebro vascular accident for the patient
4. Blood sugar recorded with in twenty four hours of the onset of stroke

Exclusion Criteria

1. Patients admitted after twenty four hours of stroke
2. Those patients who received intravenous glucose before or during study period
3. Patients with reliable information about diabetes could not be obtained
4. Patients who died before it could be established whether or not they had diabetes
5. Illness presented with stroke like symptoms

Out of the 140 patients, 20 patients were dropped as follow up could not be done. Complete history was taken, clinical examination was done and clinical diagnosis for each patient was arrived. Blood pressure measurement, blood sugar, urea, creatinine, electrolytes, hemoglobin, total count, differential count; urine sugar, albumin, deposits; electrocardiogram and chest X ray done for all patients.

The severity of stroke for each patient is calculated based on NIH stroke scale, NIHSS which takes the clinical findings in to account and each criteria awarded specific points. The points were added, with a maximum of forty two points.

Score Stroke severity

0: No stroke symptoms
1-4: Minor stroke
5-15: Moderate stroke
16-20: Moderate to severe stroke
21-42: Severe stroke

Once clinical diagnosis of acute stroke is made venous blood sample is taken, with in twenty four hours of onset of symptoms, and sent to laboratory for glucose estimation. In patients with blood sugar more than 6.1 mmol/l (110 mg/dl) and without a history of diabetes, Hemoglobin A 1c was performed. Hemoglobin A1c is structurally similar to hemoglobin A except for the addition of glucose Group to the terminal amino acid of the beta chain of the hemoglobin Molecule (glycosylation). Therefore hemoglobin A 1c is a function of the exposure of the red blood cells to glucose. Since the glucose linkage to hemoglobin is relatively stable, Hemoglobin A1c accumulates through out of the life span of erythrocyte and its concentration reflects the integrated blood glucose concentration over a period approximating to the half life of erythrocytes i.e. six to eight weeks. Therefore measurement of hemoglobin A 1c helps to monitor the overall degree of diabetic control achieved.

The normal range of Hemoglobin A 1c is 3.8% to 6.4%. Hence the patients can be classified into four groups

Group 1: Blood sugar less than 6.1 mmol/l: **Non diabetic (euglycemic)**
Group 2: History of diabetes: **Known diabetics**

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Group 3: Blood sugar more than 6.1mmol/l, no history of diabetes, and hemoglobin A1c more than 6.4%: **Newly detected diabetics**

Group 4: Blood sugar more than 6.1 mmol/l, no history of diabetes, and hemoglobin A1c less than 6.4%: **Stress hyperglycemics**

The patients were followed up for thirty days and outcome in the form of death; poor, moderate and good improvements were recorded. Patients who were unable to return to any form of work, persistent. Disability, need for residential placement, dependent in activities of daily Living, and stable deficit with no recovery were classified as those with poor outcome. Patient whose symptoms improved, who were independent in attending day to day activities, improvement in motor function and aphasia and no persistent disability were grouped as patients with good outcome. Patients who fared in between these two groups were grouped as those with moderate outcome.

Results

In our study of hundred patients majority of them belonged to male sex showing a male preponderance which is commonly seen in most studies. Majority of the patients, thirty were between the age group of 51 to 60. Among the 120 patients 64 had hypertension, 68 had diabetes, 58 had hypercholesterolemia, 6 had previous history of myocardial infarction and 2 female patients had atrial fibrillation.

More than two third of the male patients were smokers and one half had history of alcohol intake. Eight two patients had right sided weakness and thirty eight patients had left sided weakness. Among the 140 patients in our study group, 80 patients had elevated admission day blood glucose level and 40 patients had normal blood glucose values. Diabetes was noticed in 64 patients and stress hyperglycemia in another 18 patients. Stress hyperglycemia amounted to more than one third of the patients. Severity of stroke was assessed with NIH Stroke scaling system. Admission day hyperglycemic patients had a higher score when compared to Euglycemic patients, which was statistically significant. Among the admission day hyperglycemic patients, uncontrolled diabetes patients had the highest mean NIHSS. Hence an elevated blood sugar at the time of stroke resulted in severe stroke. In the ischemic stroke group early mortality rate was 2.07 % in euglycemic patients and 14.8 % in hyperglycemic patients. Poor outcome was noticed in 3.18 % in euglycemics and 38.3 % in hyperglycemics. Hence hyperglycemia was associated with an increased early mortality rate and poor functional outcome in ischemic stroke group which was also statistically significant.

A positive correlation (r=0.71) between admission day sugar value and the outcome of stroke. Higher admission day elevated blood glucose level has increased mortality and high risk of poor functional recovery was seen in the results of the study.

Table 1: Comparison of stroke severity and HBA1C Level

Stroke severity	Euglycemic	Known diabetic	Newly detected	Stress hyperglycemic
Minor	0	2	0	4

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Moderate	4	22	10	24
Moderate to severe	0	20	10	0
Severe	0	20	4	0
Total	4	64	24	28

Discussion

Stroke is 80% to 90% ischemic and 10 % hemorrhagic. Abrupt disruption of focal cerebral blood flow causes acute ischemic stroke. Acute ischemic strokes result from vascular occlusion secondary to thromboembolic disease. Ischemia causes cell hypoxia and depletion of cellular adenosine triphosphate (ATP). Diabetes mellitus is an independent risk factor for stroke and one of the important risk factors causing strokes at younger ages. The mechanism is believed to be accelerated atherosclerosis, which can Affect vessels in many distributions, including small and large vessels.[12,13]

It is an independent risk factor for stroke. It increases the susceptibility to coronary, femoral, and cerebral atherosclerosis. The relative risk increases two to fourfold in diabetic's patients with diabetic complications like retinopathy and autonomic neuropathy have a higher incidence of ischemic stroke.[13,14]

Elevated levels of triglycerides, low-density lipoproteins (LDL), and very low-density lipoproteins (VLDL), along with lower than normal levels of high-density lipoprotein (HDL), are common findings in the lipid profiles of patients with diabetes. The combined effect of these factors results in promotion of atherosclerosis and thrombosis.[15] Elevated blood glucose is common in the early phase of stroke. The prevalence of hyperglycemia, defined as blood glucose level more than 126 mg/dl has been observed in two third of all ischemic stroke subtypes on admission. Extensive experimental evidence in stroke models support that association between blood glucose and functional outcome has been found in increasing number of clinical studies.[16]

Seventeen two percent of euglycemic had a good functional recovery. On the contrary only three percent of admission day hyperglycemic patients had good functional recovery at the end of thirty day follow up.

Early inpatient mortality was high in admission day hyperglycemic patients. Fifty percent of the admission day hyperglycemic patients died within the first thirty days. In the euglycemic patients the early case fatality rate was only fifteen percent. Hence there was a three fold increased risk of early mortality in admission day hyperglycemic patients when compared to euglycemics. Poor outcome was noticed in thirty eight percent of admission day hyperglycemic patients and in three percent of euglycemic patients.

This study of fifty acute stroke patients shows that admission day elevated blood glucose level was associated with a high early mortality rate and an increased risk of poor functional recovery. These data's were statistically significant with p=0.0001.

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Hence hyperglycemia was associated with an increased early mortality rate and poor functional outcome in ischemic stroke group which was also statistically significant Our study clearly shows a positive correlation ($r=0.71$, $p = 0.01$) between admission day sugar value and the outcome of stroke. Higher admission day elevated blood glucose level has increased mortality and high risk of poor functional recovery.

Sarah E capes et al analyzed thirty two similar studies and concluded that hyperglycemic patients had threefold increased early mortality than euglycemic patients. After ischemic stroke admission hyperglycemia was associated with three fold increased 30 day mortality than euglcemics.[17]

In our study, ischemic patients, who had elevated admission day glucose level experienced a three and a half fold increased early mortality than euglycemics. Similar results were noticed in non diabetic patients. Non diabetic stress hyperglycemic patients with ischemic stroke had three and a half fold increased early mortality when compared to euglycemics. In the diabetic group since the sugar value before the onset of stroke was not known, the effect of stress in diabetic group could not be studied.

The study clearly shows an increased early mortality rate and poor functional recovery in patients with diabetes and stress hyperglycemia when compared to euglycemics. Hence there is an urgent need to confirm the improvement in these patients by normalizing blood sugar.

Several trails are now under way to improve the outcome of Stroke by normalizing the blood glucose with human recombinant insulin. Stephan M. Vinychuk et al showed that administration of insulin to patients with hyperglycemia improves functional recovery and vital activity of mild to moderate ischemic stroke patients. However, other clinical benefits of the insulin therapy remain to be determined.

Conclusion

There is a good correlation between admission day glucose level and the outcome in ischemic stroke. Admission day elevated glucose level was a significant predictor of mortality and poor functional outcome after acute stroke. Hence, restoration of normoglycemia as soon as possible should be encouraged. In the interim, we should fare well with adhering to good general stroke management, normalization of body temperature, fluid balance and hemodynamics or we may otherwise risk the favorable outcome even in the patients with normoglycemia.

References

(1) Pandian, J. D.; Sudhan, P. J. J. o. s. Stroke epidemiology and stroke care services in India. **2013**, *15*, 128.

(2) Kamalakannan, S.; Gudlavalleti, A. S.; Gudlavalleti, V. S. M.; Goenka, S.; Kuper, H. J. T. I. j. o. m. r. Incidence & prevalence of stroke in India: A systematic review. **2017**, *146*, 175.

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(3) Raghavan, K. Clinical Outcome of Stroke in relation to Admission Day Glycemic Status. Madurai Medical College, Madurai, 2012.

(4) Patil, S. A.; Reddy, H. To Study the Role of Serum Uric Acid as a Risk Factor in Acute Ischemic Stroke in Navodaya Medical College Hospital & Research Centre, Raichur. **2019**.

(5) Khaku, A. S.; Tadi, P. Cerebrovascular disease. **2017**.

(6) Arauz-Pacheco, C.; Parrott, M. A.; Raskin, P. J. D. c. The treatment of hypertension in adult patients with diabetes. **2002**, *25*, 134-147.

(7) Gorelick, P. B.; Scuteri, A.; Black, S. E.; DeCarli, C.; Greenberg, S. M.; Iadecola, C.; Launer, L. J.; Laurent, S.; Lopez, O. L.; Nyenhuis, D. J. s. Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American Heart Association/American Stroke Association. **2011**, *42*, 2672-2713.

(8) Vijay Anand, N. Clinical Outcome of stroke in relation to admission day glycemic status. Stanley Medical College, Chennai, 2007.

(9) Parthiban, S. R.; Arumugam, M. Clinical outcome of stroke with admission day glycemic status.

(10) Patel, S.; Metgud, R. J. J. o. c. r.; therapeutics. Estimation of salivary lactate dehydrogenase in oral leukoplakia and oral squamous cell carcinoma: a biochemical study. **2015**, *11*, 119-123.

(11) Metgud, R.; Naik, S.; Patel, S. J. J. o. C. R.; Therapeutics. Spindle cell lesions: A review on immunohistochemical markers. **2017**, *13*, 412-418.

(12) Brott, T.; Bogousslavsky, J. J. N. E. J. o. M. Treatment of acute ischemic stroke. **2000**, *343*, 710-722.

(13) Radak, D.; Katsiki, N.; Resanovic, I.; Jovanovic, A.; Sudar-Milovanovic, E.; Zafirovic, S.; A Mousad, S.; R Isenovic, E. J. C. v. p. Apoptosis and acute brain ischemia in ischemic stroke. **2017**, *15*, 115-122.

(14) Donkor, E. S. J. S. r.; treatment. Stroke in the century: a snapshot of the burden, epidemiology, and quality of life. **2018**, *2018*.

(15) Brewer Jr, H. B.; Santamarina-Fojo, S. J. T. A. j. o. c. Clinical significance of high-density lipoproteins and the development of atherosclerosis: focus on the role of the adenosine triphosphate–binding cassette protein A1 transporter. **2003**, *92*, 10-16.

(16) Rajman, I.; Harper, L.; Mcpake, D.; Kendall, M. J.; Wheeler, D. C. J. N., dialysis, transplantation: official publication of the European Dialysis; Association, T. A.-E. R. Low-density lipoprotein subfraction profiles in chronic renal failure. **1998**, *13*, 2281-2287.

(17) Mi, D.; Wang, P.; Yang, B.; Pu, Y.; Yang, Z.; Liu, L. J. T. a. i. n. d. Correlation of hyperglycemia with mortality after acute ischemic stroke. **2018**, *11*, 1756285617731686.