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Glycaemic Status in Acute Stroke in Nondiabetic Patient

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Abstract:

Background: *Elevated blood glucose is common in the early stage of stroke. Besides, blood glucose level increases during acute stroke in nondiabetic patients.*

Objective: *Objective of the study was to assess the glycemic status during acute stroke in nondiabetic patients, find the rate of newly developed diabetes during acute stroke and rate of newly developed Impaired Fasting Glucose, Impaired Glucose Tolerance during acute stroke.*

Methods: *The purposive sampling method was used to identify the patients and by proper history taking, documentary papers and laboratorial support evidenced by HbA1c level less than 6.5% (This means patient to be non diabetic). Data were collected from 100 patients. It was conducted from August, 2018 to February, 2019 in the Department of Medicine of Dhaka Medical College Hospital.*

The data were collected through questionnaire ,pre-tested earlier and data collection sheet illustrating the glycemic status during acute stroke among the nondiabetic patients.

Results: *While analyzing the lab investigations among the respondents, mean HbA1c level was found 5.69± 0.65 mmol/L level which was found normal among the entire patient group. Patients Fasting Blood Sugar(FBS) was tested and mean FBS level was 5.94±0.86. In 62% of the patients, IFG was found, and in 12% of patients, FBS value was found to be diabetic while 26% showed normal glycemic status. Average OGTT(2 hours after 75 gm glucose) impression was 8.53± 2.02 mmol/L. OGTT level was normal among 30%, 54% patients had IGT and 16% of the respondents were found diabetic.*

Conclusion*: The study finds that, in patients with no history of diabetes who have acute stroke, may develop moderately elevated glucose levels which may affect short term and long term stroke related morbidity and mortality.*

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Introduction:

The prevalence of hyperglycemia, defined as blood glucose level >6 mmol/L has been observed in two thirds of all ischemic stroke subtypes on admission and in at least 50% in each subtype including lacunar strokes.[1] Extensive experimental evidence in stroke models supports that hyperglycemia has adverse effects on tissue outcome. Active lowering of elevated blood glucose by rapidly acting insulin is recommended in most published guidelines, even in nondiabetic patients (European Stroke Initiative [EUSI] guidelines >10 mmol/L, American Stroke Association [ASA] guidelines >300 mg/dL).[2]

Although upto one third of acute stroke patients have either diagnosed or newly diagnosed diabetes, probably a major proportion of patients have stress hyperglycemia mediated

partly by the release of cortisol and norepinephrine. It is also a manifestation of relative insulin deficiency, which is associated with increased lipolysis.[3]

By provoking anaerobic metabolism, lactic acidosis, and free radical production, hyperglycemia may exert direct membrane lipid peroxidation and cell lysis in metabolically challenged tissue. Moderately and severely increased blood glucose has been found to further the metabolic state and mitochondrial function in the area of ischemic penumbra.[4]The evolution of an acute infarction may be expedited by the very same vascular factors, explaining why ischemia time seems to fly faster with patients with diabetes or grave hyperglycemia. Relative insulin deficiency liberates circulating free fatty acids, which, together with hyperglycemia, reportedly diminishes vascular reactivity.[5] Furthermore, lowering glucose with insulin has been reported to reduce ischemic brain damage in an animal model.[6]

The evolution of an infarction is accompanied by glutamate release mediating repeated waves of spreading depression (SD), another mechanism believed to propagate the necrosis of the penumbral tissue. Although hyperglycemia alone did not trigger early-response genes in the cortical tissue of rats, in conjunction with induced SD, the expression of c-*fos* and cyclooxygenase-2 were substantially increased.[7]

The blood-brain barrier is well known to be vulnerable to hyperglycemia, presumably through the liberation of lactic acid and free radicals. The recent experimental study by Song et al in a rat model of collagenase-induced intracerebral hemorrhage (ICH) adds that hyperglycemia aggravates edema formation in a zone surrounding cerebral hemorrhages.[8] The study also documented increased cell death measured by the TUNEL staining. It is conceivable that hemorrhages are surrounded by a zone of similarly challenged tissue as infarctions are, where the availability of glucose influences the metabolic state.

Although chronic hyperglycemia is a well-established risk factor for vascular disease, the effects of hyperglycemia during acute illnesses, such as acute cerebral infarction, are not clear. Better glycemic control during the acute phase has been shown to improve clinical outcomes from myocardial infarction,[9] A Cross sectional study was undertaken in Dhaka Medical College hospital among the patients who admitted for stroke.

Materials and Methods:

The study was carried out in Department of Medicine, Dhaka Medical College Hospital. The study period was about 6 months, which started on August, 2018 and ended in February, 2019.

Though the initial projection of respondent was 163 stroke patients. But finally respondents' number was limited within 100. Purposive sampling method was used to select the sample.

Non-diabetic patients' selected by proper history taking, documentary papers, HbA 1c level less than 6.5% (<6.5%) in both male and female of all adult age groups in acute stroke patients. Severely debiliated patients with intercurrent illness such as thyroid diseases, renal failure, heart failure, severely debiliated condition, Diabetes Mellitus patients(e" HbA1c 6.5%),patients getting drugs and glucose infusion (glucocorticoids, thiazides), patients and his or her attendants deny participate in study were excluded from the study.

Fasting blood glucose (FBS) and standard oral glucose tolerance test were done within 3 days from acute stroke patients. On the 2nd or 3rd day, fasting blood sample was drawn for estimation of plasma glucose and HbA1c. All of the remaining subjects were undergone glucose tolerance test with 75gm glucose load on the 3rd day after admission.

Two (2) cc blood from cubital vein for FBS and HbA1c was collected in a test tube containing Na-fluoride & EDTA as anticoagulant and preservative. For 2hr PPBS blood sample will be collected similarly as previous. All samples were sent to laboratory for analysis.

Subjects who had elevated glucose values at fasting (5.6-6.9mmol/l) or at 2h after glucose load (7.8-11 mrnol/1) were classified using the American Diabetic Association guide line-2017 as impaired glucose and Subjects with glucose (fasting ≥7mmol/l and / or 2h ≥1 1.1 mmoI/l) were classified as diabetic. Undiagnosed preexisting diabetes will be considered possible if the HbA1c values were >6.5%, a induced hyperglycemia will be considered if the HbA1c values <6.5%.

Statistical methods:

The collected data was checked, verified and then entered into the computer. Variations of $p < 0.05$ or less were considered to be statistically significant. The statistical analysis was done using SPSS software (version 17.0).

Results

While analyzing the age of the respondents, it was found that the study was conducted among 100 respondents of different ages between the 42 years to 78 years age range. However, their mean age was 61.76±7.33 years.

With a view to know about level of concentration of Hb1Ac and its impression to recognize the respondents as previous diabetic or not, patient's HbA1c level was calculated. The concentration of HbA1c level among the 100 respondents

was 3.00 mmol/L to 6.40 mmol/L. The average HbA1c level was 5.69± 0.65 mmol/L. In case of illustrating the impression of HbA1c, it was found that, HbA1c level was normal among the entire final respondent.

Table -I

Status and impression of HbA1c

HbA1c Level (in U/L)	Minimum	Maximum	Mean	Std. Deviation
	3.00	6.40	5.69	.65
HbA_1c Impression			Frequency	Percent
Responses	Normal		100	100.0
	Total		100	100.0

In order to analyze laboratory impression among the respondents, patients FBS (Fasting Blood Sugar) was tested. The level of FBS among the respondents ranged from 4 mmol/L to 7.93 mmol/L. The average FBS level was 5.94± .86. On basis of the FBS level analysis, the impressions were counted. It was found from the study that FBS level was normal among 26% of the respondents and in case of 62% of the respondents, IFG (Impaired Fasting Glucose) was found. On basis of FBS analysis, it was also found that 12% of the respondents were diabetic.

Table-II

Status and impression of FBS

Level of FBS (in mmol/L)	Minimum	Maximum	Mean	Std. Deviation
	4.00	7.93	5.94	.86
Impression of FBS			Frequency	Percent
Responses	Normal		26	26.0
	IFG		62	62.0
	Diabetic		12	12.0
	Total		100	100.0

With a view to know about level of OGTT and its impression, patient's OGTT level was calculated. The level of OGTT among the respondents ranged from 5.70 mmol/L to 15.10 mmol/L. The average OGTT level was 8.53± 2.02 mmol/L. On basis of the OGTT level analysis, the impressions were counted. It was found from the study that OGTT level was normal among 30% of the respondents and in case of 54% of the respondents, IGT (Impaired Glucose Tolerance) was found. On basis of the OGTT concentration, it was also found that 16% of the respondents were diabetic.

Table-III

Status and impression of OGTT

Level of OGTT (in mmol/L)	Minimum	Maximum	Mean	Std. Deviation
	5.70	15.10	8.530	2.018
OGTT Impression		Frequency	Percent	
Responses	Normal		30	30.0
	IGT		54	54.0
	Diabetic		16	16.0
	Total		100	100.0

To portray the RBS level of the respondents, the above mentioned chart has been generated. Besides, on basis of the standard value for determining the class for each value of RBS, it was found that in case of only 10 respondents, the RBS value was above 11 mmol/L. However, in case of 56 patients, the value of RBS within 7.8 to 11.0 mmol/L. In case of rest of the 34 patients, RBS value was less than 7.0 mmol/L.

Table-IV

RBS level in blood (In mmol/L)

RBS level (in mmol/L)	Frequency	Percent
Below 7.0 mmol/L	34	34.0
7.8-11.0 mmol/L	56	56.0
Above 11.0 mmol/L	10	10.0
Total	100	100.0

Discussion

Previous analysis of stroke incidence and mortality in the Oslo Study[10] after 12 years of follow-up of healthy men with no known symptoms or diseases of cardiovascular origin or diabetes showed that fasting glucose level was a significant risk factor in incidence or mortality of stroke or except in total mortality In order to analyze laboratory impression among the respondents, patients FBS (Fasting Blood Sugar) was tested. The level of FBS among the respondents ranged from 4 mmol/L to 7.93 mmol/L. The average FBS level was 5.94± .86. On basis of the FBS level analysis, the impressions were counted. It was found from the study that FBS level was normal among 26% of the respondents and in case of 62% of the respondents, IFG (Impaired Fasting Glucose) was found. On basis of FBS analysis, it was also found that 12% of the respondents were diabetic.

The level of plasma glucose is measured by means of an Oral Glucose Tolerance Test (OGTT).[11] With a view to know about level of OGTT and its impression, patient's OGTT level was calculated. The average OGTT level was

7.71± 1.75 mmol/L. The study finds that in case of 54% of the respondents, IGT (Impaired Glucose Tolerance) was found. On basis of the OGTT concentration, it was also found that 16% of the respondents were diabetic. However, once IGT has developed, the body's insulin secretion and sensitivity tend to continue to decline, ultimately resulting in type 2 diabetes.

A similar study[12] was done by Division of Diabetic Medicine and Endocrinology and Department of Medicine, Groote Schuur Hospital, Cape Town, South Africa from July 2004 to 2006.In that study One hundred and seven patients were analysed. Our study differs from that study only in few aspects. Study period was long in Cape Town study and they also observed whether any persistence hyperglycemia or not in future. They also observed the lipid profile of the patients what we did not.We considered the cut off value of HbA1c < 6.5% instead of <7% and measured IFG which differs from that. Rest of the study is almost similar to our study. Among 107 patients, sixty-five patients (61%) were dysglycaemic [26 (24%) had diabetes and 39 (37%) had IGT] and 42 (39%) had NGT. The percentage of newly developed hyperglycemia was little bit lower than our study as we found 70% patient with abnormal glycemic status.

Another similar study was carried out by Venchuri et al[13] in 2005 in Italy where the percentage of developing stroke induced hyperglycemia in non-diabetic patients was higher than our study .In that study eighty-one patients (84.4%) out of 97 , had abnormal glucose metabolism during discharge and 62 (64.6%) after 3 months. Thirty-seven (38.5%) had impaired glucose tolerance at discharge and 26 (27.1%) after 3 months. Forty-four (45.8%) had diabetes at discharge, and 36 (37.5%) at 3 months.

Abnormal results of HbA1c means that blood glucose levels have not been well controlled over a period of weeks to months. If HbA1c is above 6.5%, it means that diabetes control may not be as good as it should be.[14-15] while measuring the level of concentration of HbA1c and its impression, patient's HbA1c level was calculated. The average HbA1c level was 5.69±0.65 mmol/L. In case of illustrating the impression of HbA1c, it was found that, the level was normal among the entire respondents. Since our study used HbA1c to screen for undetected diabetes, the possibility of underlying diabetes as explanation of hyperglycemia seen after stroke may not be valid for patients.

As the blood glucose test is performed to monitor the level of glucose in the blood and hence detect both hyperglycemia and hypoglycemia, which helps in the diagnosis of diabetes mellitus and even also in case of acute stroke patients.[16]To portray the RBS level of the respondents, the above mentioned chart has been generated. Besides, on basis of the standard value for determining the class for each value of RBS ranged in between 5.10 to 13.06 mmol/L. It was noteworthy that, in case of 10 respondents, the value of RBS was ≥11.1 mmol/L.

Conclusion:

The study finds that, in patients with no history of diabetes who have acute stroke, may develop moderately elevated glucose levels which may affect short term and long term stroke related morbidity and mortality. We should create awareness about a new risk factor–acute hyperglycemia during acute stroke and take appropriate and effective measures to reduce morbidity and mortality.

Conflict of interest: None

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