Research Article

The incidence of stress hyperglycemia in acute ischemic stroke patients (in Al-Yarmouk teaching hospital)

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Abstract

Aims: Stress hyperglycemia represents a transient increase in blood glucose in reaction to acute illness. Cases with stress hyperglycemia have higher mortality rates and worse functional outcomes than the ones with known diabetes or normoglycemia. This study evaluated the incidence of stress hyperglycemia in acute ischemic stroke patients and its relationship with stroke risk factors.

Patients and Methods: WHO criteria is used to confirm hyperglycemia and HbA1c test to detect stress hyperglycemia in a sample of 220 patients with acute ischemic stroke who were admitted to Al-Yarmouk teaching hospital in Baghdad from 1 April to 31 December 2010.

Results: thirty nine patients with acute ischemic stroke had stress hyperglycemia. There is significant effect of gender, hypertension, atrial fibrillation and dyslipidemia on patients with stress hyperglycemia while this is not found with obesity and smoking.

Conclusions: stress hyperglycemia is a common phenomenon in patients who develop acute ischemic stroke.

Keywords: Incidence, Stress hyperglycemia, Acute ischemic stroke

INTRODUCTION

Stress hyperglycemia is usually defined as hyperglycemia resolving spontaneously after dissipation of acute illness. The term generally refers to patients without known diabetes, although patients with diabetes might also develop stress hyperglycemia a fact overlooked in many studies comparing hospital in patients with or without diabetes. Investigators of several studies suggest that patients with stress hyperglycemia and no previous diagnosis of diabetes face worse consequences at a given severity of hyper glycaemia than do those with pre-existing diabetes.[1]

Some evidence suggests that chronic hyperglycemia sets up a pattern of cellular conditioning that might actually be protective of acute hyperglycemia-mediated damage during critical illness. One mechanism for this effect might be the preferential down regulation of glucose transporters under conditions of chronic rather than intermittent hyperglycemia.[2, 3]

It is not clear whether a high blood glucose concentration is independently associated with poor prognosis or it indicates more severe underlying illness with an augmented response to stress.[4, 5, 6] In cases of acute ischemic stroke, admission hyperglycemia is associated with a poorer functional outcome, longer hospital stay, and higher risk of death within 30 days, even in patients without diabetes.[7]

In the hospital setting, a combination of factors affects the development of stress hyperglycemia. The mechanisms for this disorder probably vary with the patients' underlying glucose tolerance, type and severity of disease, and stage of illness. However, the development of stress hyperglycemia is caused by a highly complex interplay of counter-regulatory hormones such as catecholamines, growth hormone, cortisol, and cytokines.[3]

The underlying illness might affect the scale of cytokine production and hormonal derangements. Complex

feedforward and feedback mechanisms between hormones and cytokines exist and this neurohormonal environment ultimately leads to excessive hepatic glucose production and insulin resistance.[8] High hepatic output of glucose, especially through gluconeogenesis, seems to be the most important contributor to stress hyperglycemia.[9]

Excessive glucagon is the primary mediator of gluconeogenesis, although epinephrine and cortisol also contribute. Tumor necrosis factor-α (TNFα) might promote gluconeogenesis by stimulating glucagon production. Insulin resistance during illness is characterized by an inability to suppress central hepatic glucose production.[10]

Hyperglycemia exacerbates the cytokine, inflammatory, and oxidative stress response, potentially setting up a vicious cycle whereby hyperglycemia leads to further hyperglycemia. Resolution of hyperglycemia is associated with normalization of the inflammatory response.[11]

Insulin resistance ultimately promotes a catabolic state in which lipolysis takes place. Excessive circulating free fatty acids in turn exacerbate insulin resistance by disrupting end-organ insulin signaling and glycogen synthase. This lipotoxicity aggravates the inflammatory state, paralleling the effects of glucotoxicity. Glucotoxicity, lipotoxicity, and inflammation are key components of what might be viewed as an exaggerated global insulin-resistance syndrome associated with acute illness. These components also promote endothelial dysfunction, which has a complex reciprocal cause–effect relation with insulin resistance.[12]

Hyperinsulinaemia might impart additive consequences to that of hyperglycemia, including exaggerated inflammatory and counter–regulatory hormone responses and impaired fibrinolysis.[13]

There are no definitive approved criteria for diagnosis of patients with stress hyperglycemia. In a meta-analysis done by Capes S.E. et al. of Canada in 2001,[7] thirty two studies of stress hyperglycemia done between1976-1994 were identified and there were different cut off points of blood glucose level been chosen to define stress hyperglycemia as fasting or random types according to each study. The levels of fasting plasma glucose (FPG) in the morning on the day after admission varies between that > 6.1mmol/dl (109.8 mg/dl) in Candelise L.et al. of Italy study in 1985[14] and >7.8 mmol/dl (140.4 mg/dl) in another study done later by Woo J.et al. of Hong Kong in 1990[5] while the random plasma glucose (RPG) drawn on admission and used to define stress hyperglycemia was between >6 mmol/dl (108mg/dl) in Stig- JØrgensen H.et al. of Denmark study in 1994[15] and >10mmol/dl (180 mg/dl) in Tuhrim S.et al. of Canada study in 1991.[16]

It should be noted that using glycated hemoglobin A (HbA_{1c}) for diagnosis is still a recommendation and is not approved by World Health Organization (WHO) as a guideline because HbA1c values can be falsely increased or decreased in some medical conditions although it has some logistical advantages over a time consuming oral glucose tolerance test or FBS as patients do not need to fast. In 2009, an International Expert Committee recommended that HbA1c of 6.5% as a cut point to diagnose diabetes mellitus and this has been approved by the American Diabetes Association but not yet by WHO.[17]

Most human studies did not mention a relation between hyperglycemia and intracerebral hemorrhage, but Bruno et al study in 2002 showed that higher admission glucose level, in acute ischemic stroke predisposes for symptomatic intracerebral hemorrhage even without thrombolytic treatment.[18]

PATIENTS AND METHODS

This is a cross sectional retrospective study of 220 adult patients with acute ischemic stroke admitted to the medical wards of Al-Yarmouk Teaching Hospital, Baghdad, during the period from 1 April until31 December 2010. The patients were divided in to 139 males and 81females with male to female ratio of (1.72:1). Their age ranges from 31 to 86 years with a mean of 61.73.

Full medical history was taken from each patient and we collected clinical information regarding the following vascular risk factors: age, gender, hypertension, atrial fibrillation, dyslipidemia, obesity and smoking. Hypertension was defined as patients with known hypertension and/or taking anti-hypertensive medication. Atrial fibrillation was diagnosed and confirmed by Electrocardiogram. Dyslipidemia was determined according to the National Cholesterol Education Program Adult Treatment Panel III guidelines.[19] Obesity was determined by measuring waist circumference of patients (>88 cm for women and > 102 cm for men). BMI is not calculated due to technical difficulties. Cigarette smoking status was classified as smokers and non-smokers. The presence of diabetes depended on the patient's reported history of treated diabetes mellitus or the presence of

HbA1c ≥ 6.5%.[17] Drug history including history of steroid intake or other diabetogenic drugs or dextrose containing fluids. Patients who received corticosteroids or dextrose water infusion were excluded so were diabetic patients.

The WHO criteria of blood glucose for diagnosis of diabetes mellitus are used to define the minimum cut- off point for hyperglycemia as RPG ≥ 140 mg/dl. HbA1c cut point of 6.5% is used according to the recommendation of International Expert Committee in 2009.[17] If patients had no history and/or signs or symptoms of diabetes we did HbA1c and if HbA1c value was less than 6.5% that means stress hyperglycemia. We divided patients into three groups, diabetic, normoglycemic and those with stress hyperglycemia.

Random plasma glucose was taken in the emergency department at the patient arrival and was performed by using enzymatic and colorimetric method GOD/POD.

HbA1c is determined by variant hemoglobin AK program using ion exchange High Performance Liquid Chromatography (HPLC) using (Variant TM Hemoglobin A1c Programs by BIO- RAD laboratories USA) which has been certified by National Glycohemoglobin Standardization Program.

CT scan and/or MRI reports were fully assessed to choose those patients with ischemic stroke.

Statistical analysis

Baseline demographic and laboratory data were expressed as mean ± standard deviation for continuous variables and as frequencies for categorical variables by t-test and x^2-test. In all tests p-value <0.05 was considered significant. All statistical analyses were conducted using the Microsoft Excel 2010 package for Windows7 (Microsoft company, USA).

RESULTS

Among 220 patients with acute stroke admitted to the hospital, 179 patients (81.3%) with ischemic stroke where included while 41 patients (18.6%) were excluded due to hemorrhagic stroke and other causes like incomplete data and death.

The included patients were divided in to 58 (32.4%) female patients and 121 (67.6%) male patients. Seventy six (42.4%) of patients with ischemic stroke were hyperglycemic with 48 (63.2%) of those with hyperglycemia were diabetic and 28 (36.8%) patients were considered to have stress hyperglycemia. Female patients with stress hyperglycemia were 15 (53.6) in comparison to 13 (46.4%) of male and there was significant difference (p=0.004). as in tables (1), (2), (3) and Fig. (1), (2).

Table 1. Demographic findings of acute ischemic stroke patients.

	Normoglycemia N=103 [%]	Stress hyperglycemia N=28 [%]	Diabetes mellitus N=48 [%]	P-value
Age	63.6±12.1	60±10.3	61.4±11.39	0.152
Gender (female: male)	26:77	15:13	17:31	0.004
Admission (RPG)	116.7±18.2	163±40.3	240.6±91.7	<0.001
HBA1c	---	5.3±0.32	---	
Hypertension	52 [51]	20 [71.4]	16 [33.3]	0.048
Atrial fibrillation	16 [15.5]	9 [32.1]	11 [22.9]	0.047
Obesity	43 [41.7]	7 [25]	21 [43.7]	0.105
Dyslipidemia	27 [26.2]	13 [46.4]	32 [66.7]	0.039
Smoking	70 [68]	15 [53.6]	31 [64.6]	0.157

Table 2. Distribution of acute Ischemic stroke patients in different groups.

Group	No.	[%]
DM	48	26.8
Normoglycemia	103	57.4
Stress Hyperglycemia	28	15.6
Total	179	81.4

Table 3. The Gender distribution of acute Ischemic stroke patients in different groups.

Group	Female		Male	
	No.	[%]	No.	[%]
DM	17	35.4	31	64.6
Normoglycemia	26	25.2	77	74.8
Stress hyperglycemia	15	53.6	13	46.4
Total	58	32.4	121	67.6

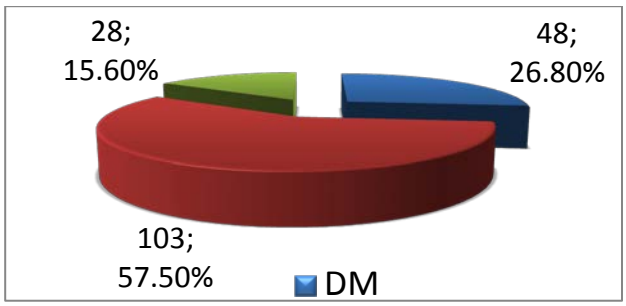

Figure 1. Pie chart of the glycemic status in different groups of ischemic stroke patients.

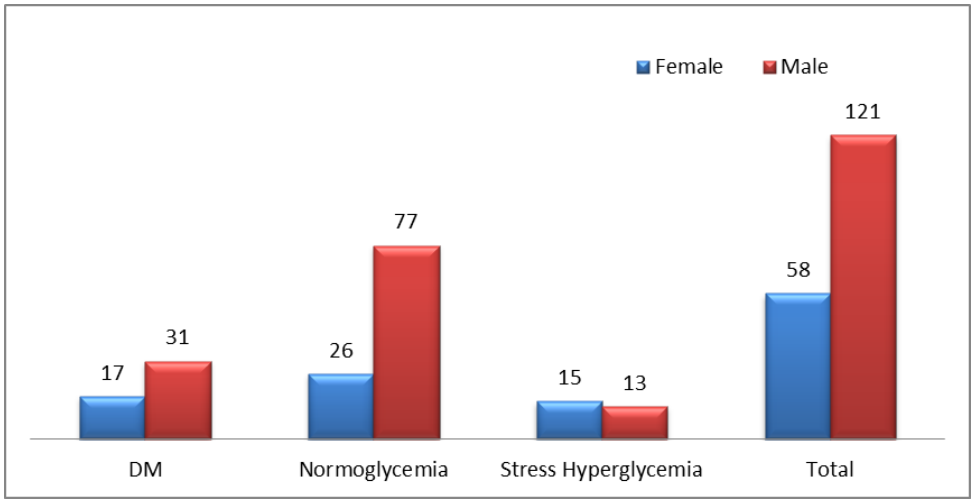

Figure 2. The Gender distribution of acute Ischemic stroke patients in different groups.

There is no effect of age on stress hyperglycemia in patients with ischemic stroke (p= 0.152) as shown in table (4).

Table 4. The age distribution of acute Ischemic stroke patients in different groups.

Age (year)	DM		Normoglycemia		Stress Hyperglycemia	
	No.	[%]	No.	[%]	No.	[%]
<40	2	4.2	5	4.8	-	-
40-50	7	14.5	6	5.8	5	17.8
50-60	9	18.7	27	26.2	10	35.7
60-70	18	37.5	33	32	7	25
70-80	12	25	24	23.3	6	21.4
>80	-	-	8	7.7	-	-
Total	48	26.8	103	57.5	28	15.6
Mean+ SD	61.4±11.39		63.6±12.1		60±10.3	

Hypertension has a significant effect on patients with stress hyperglycemia (p=0.048). Twenty (11.17%) from total ischemic stroke patients had stress hyperglycemia with hypertension and compose (71.4%) of total patients with stress hyperglycemia as in table (1).

The number of patients who had atrial fibrillation and ischemic stroke with stress hyperglycemia was (9) (5%) of total ischemic stroke patients which represent (32.1%) of patients with stress hyperglycemia. There is a significant statistical relation between atrial fibrillation and stress hyperglycemia (p=0.047) as in table (1).

Seven (3.9%) of patients with stress hyperglycemia and ischemic stroke had obesity and constitute (25%) of total patients with stress hyperglycemia so that obesity is not a significant predisposing factor for stress hyperglycemia as in table (1).

Thirteen (7.3%) of total ischemic stroke patients had dyslipidemia and stress hyperglycemia which equals to (46.4%) of total patients with stress hyperglycemia with a significant influence on initiation of stress hyperglycemia (p=0.039) as in table (1).

Smokers with ischemic stroke and stress hyperglycemia were (15) (8.4%) of total patients with ischemic stroke, and equal to (53.6%) of total patients with stress

hyperglycemia so smoking is not a significant predisposing factor for the stress hyperglycemia (p=0.157) as in tables (1) and (5).

Table 5. The smoking habits of acute Ischemic stroke patients in different groups.

Group	Smoker		Non Smoker	
	No.	[%]	No.	[%]
DM	31	64.6	17	35.4
Normoglycemia	70	68	33	32
Stress hyperglycemia	15	53.6	13	46.4
Total	116	64.8	63	35.2

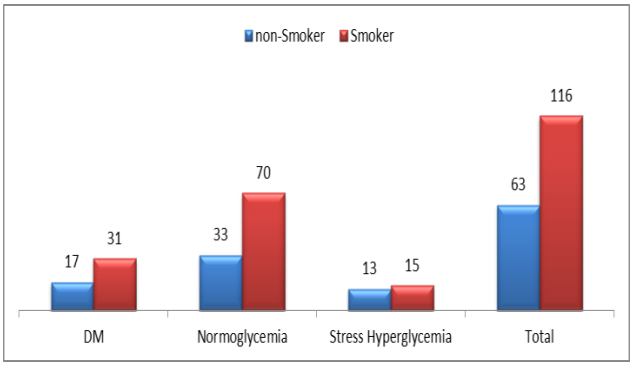

Figure 3. The smoking habits of acute Ischemic stroke patients in different groups.

DISCUSSION

Hyperglycemia is common in patients with acute stroke occurring in up to 60% of them.[20, 21] In this study, 42.4% of all ischemic stroke patients admitted to the hospital were hyperglycemic and 15.6% of ischemic stroke patients having stress hyperglycemia. This percentage goes with many studies done worldwide of acute stroke patients without a prior diagnosis of diabetes which was between 8% as in a study by Kiers I. et al. of Australia study in 1992[22] and 63% in another study done earlier by Cazzato G. et al. of Italy study in 1991.[23] The difference between studies depends on their definition of stress hyperglycemia.

There is increase in the incidence of stress hyperglycemia in females with a percentage of 53.6% which is statistically significant and is similar to what was found in Bravata D.M. et al of USA[24] study which showed preponderance of women (54%) among admitted hyperglycemic patients with acute ischemic stroke.

No relation was found between smoking and stress hyperglycemia and this agrees with Heo S.H. et al. of Korea study in 2010[25] and Dziedzic T. et al. of Poland study in 2010[26] while there is no agreement between our study and other studies regarding age and obesity.

There is a strong relation between hypertension, atrial fibrillation and dyslipidemia with stress hyperglycemia in this study and this was also found by Gray C.S. et al. of UK study in 2004.[27]

Many studies worldwide like those done by Szczudlik, A. et al in Poland 2001[20] Capes, S.E. et al.[7] and Dora B. et al. in Turkey 2004[28] showed that patients with stress hyperglycemia had higher stroke severity, worse clinical outcome and adverse effect on short term prognoses. In our study we did not follow up patients so we cannot state the relationship between stress hyperglycemia and prognosis.

Conflict of interest: none

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