

# Stress Hyperglycemia As a Predictor of Adverse Outcome in Patients with Acute Ischemic Stroke: Should We Care?

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Stroke is the second leading cause of disability and death worldwide and is particularly higher in low- and middle-income countries [1]. In 2022, it is estimated that 1 in 4 deaths from cardiovascular disease is due to stroke [2]. An estimation from a meta-analysis indicated that stroke recurrence was 11 % and 26 % within 1 and 5 years respectively in 2011 [3]. The latest meta-analysis concluded that the rate of stroke recurrence has not changed over the last decade [4]. Therefore, it is important to prevent stroke recurrence by improving secondary prevention especially during acute care.

Studies have found several predictors of adverse outcome in patients with acute ischemic stroke (AIS) [5 - 7]. One of those is stress hyperglycemia which is a transient elevation of the blood glucose or acute spikes in hyperglycemia due to the stress of illness. The increased blood glucose level results from a release of stress hormones such as cortisol and catecholamines due to stress stimulation in the hypothalamus-pituitary-adrenal axis during AIS [8]. As concluded in systematic reviews, tissues are somehow protected in diabetic subjects compared to non-diabetic subjects (as known here stress hyperglycemia) during acute spike of hyperglycemia in AIS patients inducing an increase of antioxidant defenses through oxidative stress in chronic hyperglycemia in diabetic subjects [9 - 11]. Therefore, stress hyperglycemia is associated with stroke severity and adverse outcomes, especially in non-diabetic subjects [12, 13]. For instance, a retrospective study including 414 AIS patients who were treated with IVT showed that significantly increased risk of poor outcome, mortality and symptomatic intracranial hemorrhage was observed in patients with severe stress hyperglycemia [12]. Another study compared the incidence of 90 - day stroke recurrence in 4 groups including patients without diabetes, newly and previously diagnosed diabetic subjects and non-diabetic subjects with stress hyperglycemia. The results showed that the patients with stress hyperglycemia had a higher cumulative incidence of stroke recurrence compared to other groups which was a 5.3 - fold increased risk of 90-day stroke recurrence after adjusting for confounding covariates [13].

In the assessment of stress hyperglycemia, it is critical to develop an expediency tool in

clinical practice [5, 13]. A recently recommended measure, the ratio of glucose to glycated hemoglobin (HbA1c), is calculated as plasma glucose in mg/dl divided by glycated hemoglobin in percent (%) [5]. HbA1c corresponds to an estimated blood glucose level for last three months which can be used in the identification of diabetes whether in people having undiagnosed diabetes or non-diabetic. Recent studies have found that the ratio of glucose to HbA1c, compared with significantly high plasma glucose levels, is the best predictor of the clinical outcome in several acute diseases like AIS in the emergency department [12 - 14].

In Mongolia, the incidence and deaths of stroke has increased significantly over the past few decades. The estimated stroke cases in 1978 and 1998 were 0.72 and 2.96 per 1,000 people, respectively [15]. According to the latest report of the World Health Organization, Mongolia is the highest rated country in the Western Pacific and the second-highest rated country in the world (196.83 / 100000) [16]. In Mongolia, no studies have investigated the relationship between acute spikes in hyperglycemia and stroke severity and adverse outcomes. We expected that Mongolians might have a higher risk of adverse stroke outcomes, especially recurrent stroke, with one explanation being stress hyperglycemia. Therefore, it might be important to determine the ratio of glucose to HbA1c during AIS in Mongolian hospitals. This may also potentially be specified in the clinical recommendations relating to secondary prevention of stroke patients. Moreover, studies should test the association between stress hyperglycemia and stroke within a broader context that encompasses transient elevation of the blood glucose in non-diabetic subjects or acute spikes in hyperglycemia as presenting newly diagnosed patients with diabetes.

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