

Original Research Article

Glycaemic levels as an independent predictor of outcome in acute ischemic stroke from a tertiary care hospital, Nellore, India

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ABSTRACT

Background: Stroke is one of the most important causes of long-term disability and the second leading cause of death worldwide. Increasing interest has been focused on the role of hyperglycaemia in the evolution of acute ischaemic stroke because of its risk on stroke outcome and also hyperglycaemia occurs in 30-40% of patients with acute ischaemic stroke; most of these individuals do not have a history of diabetes mellitus.

Methods: This study subjects consisted of 100 consecutive patients who presented to the Narayana Medical College and Hospital, Nellore with acute ischaemic stroke within 24 hrs of symptom onset and had capillary blood glucose (CBG) measured on presentation. Patients with hyperglycaemia (CBG>140 mg/dl) were then stratified into those with stress hyperglycaemia, newly detected diabetes mellitus and with pre-existing diabetes mellitus for the purpose of analysis. The outcome of stroke in terms of functional impairment and 90-day mortality were studied.

Results: Patients with hyperglycaemia exhibited significantly greater functional impairment ($p<0.0001$) than those with normoglycemia. The outcome was poor in patients with hyperglycaemia. Stroke severity ($p<0.001$) and functional impairment ($p<0.001$) were both significantly worse in patients with Hyperglycaemia and no prior history of DM; when compared to a patient with hyperglycaemia and previously diagnosed DM.

Conclusions: This study concludes that hyperglycaemia at stroke onset is associated with a higher risk of poor outcome independent of the other variables. Patients with hyperglycaemia at stroke onset, without prior history of DM, have a particularly poor prognosis, then that of patients with known diabetes. Thus, hyperglycaemia is not solely a stress response to neurological insult, as it predicts outcome. Hence, hyperglycaemia needs to be treated to have reduced morbidity and mortality pertaining to stroke outcome.

Keywords: Acute ischemic stroke, Diabetes mellitus, Hyperglycaemia

INTRODUCTION

World health organization defines the clinical syndrome of stroke as rapidly developing clinical signs of focal or global disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than a vascular origin.¹ The majority of stroke is ischemic type, while the remaining result from primary haemorrhage in intracerebral or subarachnoid space.² Of the many factors like subtype and severity of the stroke, which alter the outcome of stroke, hyperglycaemia predicts higher mortality and morbidity.³

The relation between disturbed glucose metabolism and ischemic stroke is bidirectional. On the one hand, people with diabetes have more than double the risk of ischemic stroke after correction for other risk factors, compared to people without diabetes. On the other hand, acute stroke can give rise to abnormalities in glucose metabolism, which in turn could affect the outcome.⁴ The hyperglycaemia in acute ischemic stroke could be either due to pre-existing diabetes or newly detected diabetes or stress hyperglycaemia. The adverse effect of hyperglycaemia is possibly due to anaerobic metabolism of glucose, worsening the intracellular and extracellular

acidosis.⁵ Diabetes also favours atherogenesis because of various lipid abnormalities like hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol and high triglycerides-enriched HDL. Stress hyperglycaemia resolves spontaneously after dissipation of the acute illness.⁶ The stress reaction that results in hyperglycaemia is initiated by activation of the hypothalamic-pituitary-adrenal axis, which leads to raised amounts of glucocorticoids and activation of the sympathetic autonomic nervous system. Increased levels of stress hormones stimulate glucose production by glycogenolysis, gluconeogenesis, proteolysis, and lipolysis. Augmented epinephrine also can result in insulin resistance and hyperinsulinemia.⁷ Impaired recanalization, decreased reperfusion, reperfusion injury and direct tissue injury are several mechanisms that have been identified through which Hyperglycaemia could aggravate cerebral damage in ischemic stroke. The increased risk is independent of other predictors of poor outcome. The present study was undertaken in a prospective manner to evaluate the effect of glycaemic status on the outcomes of stroke.

METHODS

The present study is a prospective longitudinal study carried out in Narayana Medical College and Hospital, Nellore, from October 2018 to March 2020. A total of 100 patients, aged 18 years and above, fulfilling the inclusion criteria were included in this study, with inclusion criteria being, the patients who presented with acute ischemic stroke within 24 hours of symptom onset and has blood glucose measured on presentation. Patients presenting with haemorrhagic stroke and recurrent stroke were excluded. Patients who presented with clinical features of acute ischemic stroke were confirmed by using computed tomography (CT) / magnetic resonance imaging (MRI) scan of the brain. The demographic, detailed history regarding the temporal profile of stroke and risk factors like hypertension (HTN), diabetes mellitus (DM), smoking, alcohol intake, previous history of strokes followed by thorough clinical examination and laboratory details (complete hemogram, serum urea, serum creatinine, random blood sugar (RBS)/ capillary blood glucose (CBG), fasting blood sugar (FBS), post prandial blood sugar (PPBS), HbA1c and fasting lipid profile) were collected in a pretested proforma. Patients were stratified into normoglycemic (CBG<140 mg/dl) and hyperglycemic (CBG>140 mg/dl) and patients with hyperglycemia were again subdivided into those with and without prior history of Diabetes.

National Institutes of Health stroke scale was used for the neurological examination to assess stroke severity. Functional impairment was assessed by using the Modified Rankin Scale (MRS) at the time of admission, discharge and at 90 days of follow up.

The descriptive statistics were used to summarize the data. All the statistical analysis were done using SPSS,

version 25.0. The graphs were made using Microsoft Excel.

RESULTS

In this study, 4% of the patients belonged to age <40 years, 15% to age group 41-50 years, 34% to age group 51-60 years, 31% to age group 61-70years and 4% to age group >80 years. Majority of the patients belonged to the age group between 51-60 years of age (Figure 1).

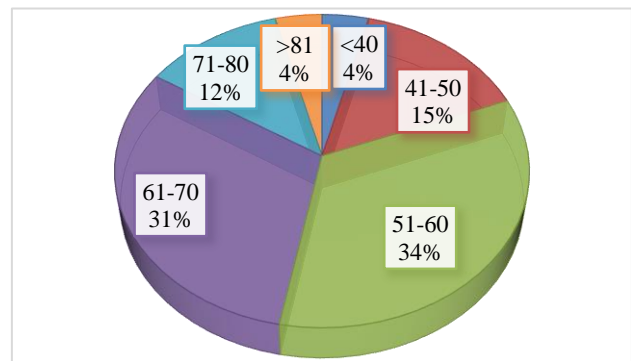


Figure 1: Distribution of age.

Out of 100 acute ischaemic stroke patients, 62 were males, and 39 were females. The presentation of stroke was higher in male sex when compared to female sex (Figure 2).

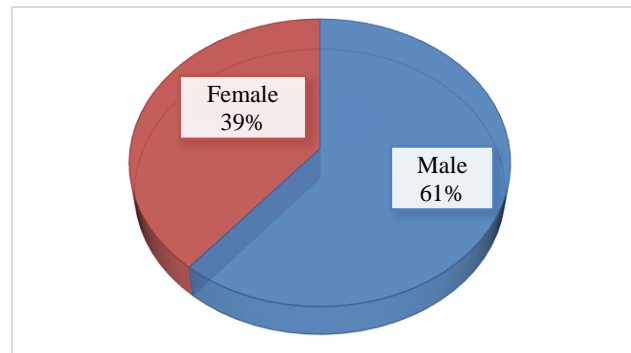


Figure 2: Distribution of sex.

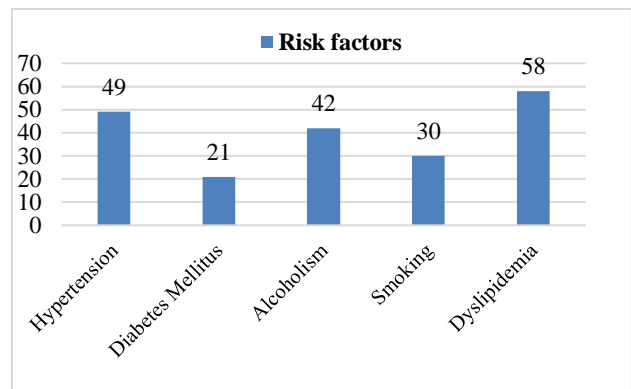


Figure 3: Risk factors in stroke.

In this study, 49 patients had a history of hypertension; 21 patients had a history of diabetes mellitus; 42 patients had a history of alcohol intake, 30 had a history of smoking. Dyslipidaemia was present in 58 patients (Figure 3).

In the present study, the majority of the patients presented with moderate stroke. In total, 25% of patients had a minor stroke, 42% of patients had a moderate stroke, 33% moderate severe stroke at the time of presentation (Figure 4).

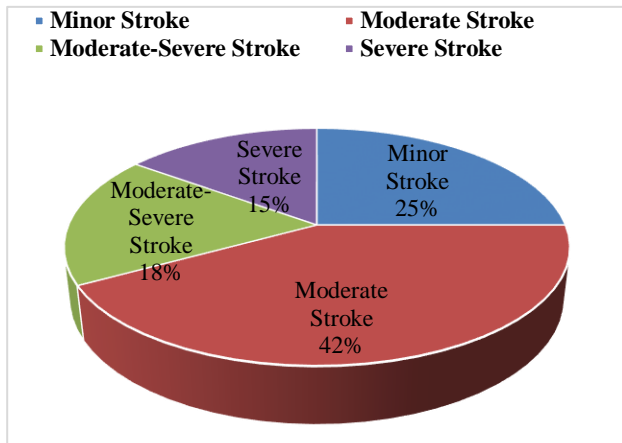


Figure 4: Severity of stroke.

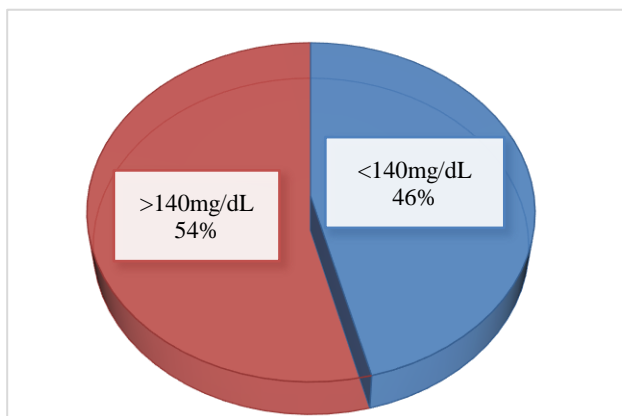


Figure 5: Blood glucose levels at the presentation of stroke.

In this study, CBG was measured at the presentation of stroke.

A total of 54% patients had hyperglycaemia with glucose levels >140 mg/dl, and 46% of patients had normoglycaemia with glucose levels <140 mg/dl (Figure 5).

Out of 100 acute ischemic stroke patients who were included in this study, 56% of the patients had hypertension with blood pressure levels measuring more than 140/90 mmHg, and 44% of patients had blood pressure levels less than 140/90 mmHg (Figure 6).

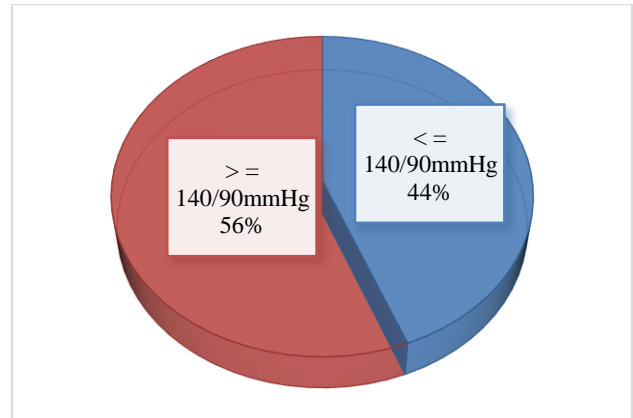


Figure 6: Blood pressure levels at the presentation of stroke.

In the present study, 45% patients were normoglycaemic, and 21% had stress hyperglycaemia, 16% were newly detected diabetics, 18% patients were diagnosed to be having DM prior to the event of a stroke (Figure 7).

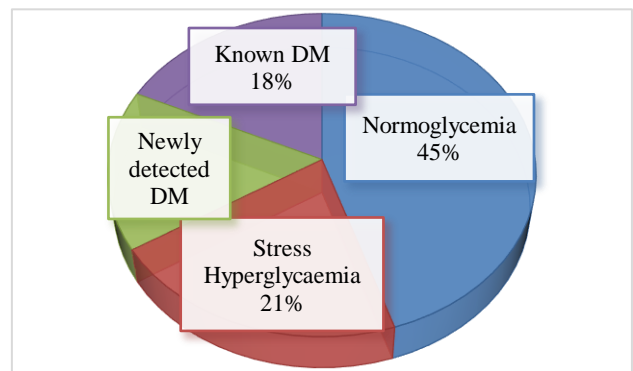


Figure 7: Glycaemic levels.

Out of total of 100 patients who were admitted with acute ischemic stroke, lipid levels were measured. It showed that 58% of patients had dyslipidaemia, and 42% had normal lipid levels (Figure 8).

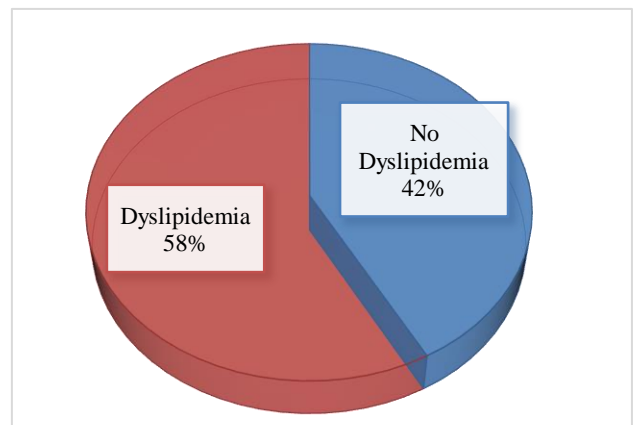


Figure 8: Lipid profile.

In the present study, Stroke severity was measure using Modified Rankin Scale (MRS). In stroke patients, 57% of them had severe stroke-related disability after 90days of the stroke event, while 43% of them had less severe stroke related disability (Table 1).

Table 1: Stroke severity after 3 months.

Stroke severity after 3 months	Number of cases	Percentage
≤3	57	57
>3	43	43
Total	100	100

Patients who presented with acute ischemic stroke, functional impairment was measured using the Modified Rankin Scale (MRS). A 68.5% of patients had an MRS score of 5 and 41.2% patients of had an MRS score of 4. These patients who had MRS score of 5 and 4, were associated with poor outcome at 90 days follow up (Figure 9).

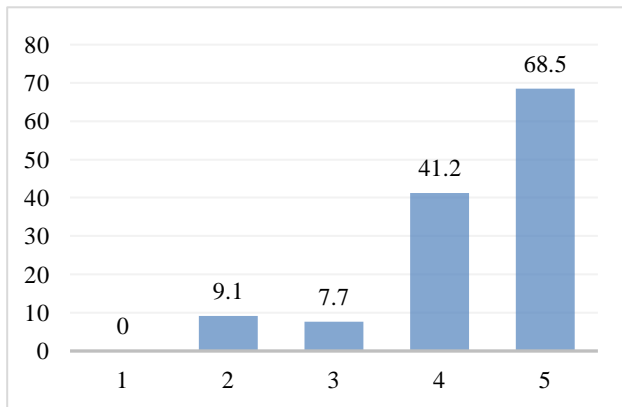


Figure 9: MRS at presentation.

At discharge, functional impairment was again assessed to all the patients. It showed that 63.2% patients of MRS score 5 and 53.8% patients of MRS score 4 were associated with poor outcome at 90 days follow up. (Figure 10).

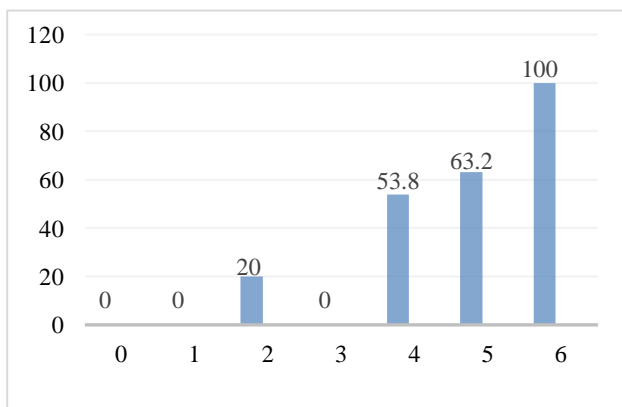


Figure 10: MRS at discharge.

DISCUSSION

Stroke is one of the important cause of long term disability and the second leading cause of death worldwide. Hyperglycaemia arises in 30-40% of patients with acute ischemic stroke, most of these individuals do not have a history of diabetes mellitus, most often it is the result of an acute stress response (stress hyperglycaemia). Studies suggest that this is not a benign occurrence and stress-induced hyperglycaemia is associated with a high risk of morbidity and mortality.

Age is the single most important risk factor for stroke. In the present study, 61% were males, and 39% were females. Males were at a greater risk for stroke than women, which are similar to the studies done by Stead et al and Kostulas et al.^{8,9} In the present study, the majority of the patients (92%) were in the age group of 41-80 years with a mean age of 60.61 years. In comparison to Stead et al and Kissela et al, the mean age for stroke is relatively low in this study.^{8,10} It is possibly because of a lack of awareness regarding various risk factors of stroke at the population level. The various risk factors associated with stroke in this study were hypertension 49%, diabetes mellitus 21%, alcoholism 42% and smoking 30%. These observations correlate well with the studies done previously by Kostulas et al and Megherbi et al.^{9,11} The observation in the present study that dyslipidemia was present in 58% of the patients is more than the study done by Hussain et al.¹²

The observation in this study, that hyperglycaemia at the time of presentation was seen in 54%, which is higher than to Baird et al, Stead et al and Lindsberg et al, observed elevated blood glucose is common in the early phase of stroke.^{8,13,14} The prevalence of Hyperglycaemia has been observed in two-thirds of all ischemic stroke subtypes on admission. Although up to one-third of acute stroke patients have either diagnosed or newly diagnosed Diabetes, probably a major proportion of patients have stress hyperglycaemia mediated partly by the release of cortisol and norepinephrine. The observation in the present study that stress hyperglycaemia was present in 21% of patients, less than in studies done by Melamed et al and Toni et al.¹⁵

In the present study, overall, 43% of the patients had poor outcome at 90 days, it appeared that those with normoglycemia had minimal functional impairment compared to patients with hyperglycaemia (p<0.0001). Among all these three subgroups of hyperglycaemic individuals, the patients with stress hyperglycaemia are associated with 85.7% worse outcome, followed by the individuals with newly detected diabetes mellitus 87.5%, and those with the previous history of diabetes mellitus are associated with 66.7% worse outcome at the end of 3 months.

In the study, Stead et al, the outcome of functional outcome (MRS) was assessed overall; it appeared that

those with normoglycemia did worse (poor MRS=53.7% (normoglycemia) vs 39.5% (hyperglycaemia), p value <0.004).⁸ In particular, among the patients without a history of diabetes mellitus, patients with elevated glucose were more likely to have a poor MRS, whereas among the patients with a history of diabetes mellitus there was no clear impact of hyperglycaemia on the poor functional outcome (MRS).

In the Capes et al, study, the patients without Diabetes, stress hyperglycaemia was associated with a 3-fold increased risk of mortality after stroke (pooled relative risk, 3.07; 95% CI, 2.50 to 3.79). In patients with diabetes, stress hyperglycaemia was not associated with a significantly higher risk of short-term mortality after stroke (pooled relative risk, 1.30; 95% CI, 0.49 to 3.43).

CONCLUSION

In this study, we found that hyperglycaemia at the time of presentation with acute ischemic stroke conferred worse prognosis. Patients with hyperglycaemia without a history of diabetes mellitus have a particularly poor prognosis than that for patients with known diabetes. In this study, the patients with hyperglycaemia had significantly more severe stroke (MRS>3).

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Ethical approval: The study was approved by the Institutional Ethics Committee

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