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# Association between Fasting Blood Glucose-HbA1c Ratio with Independence Status and Clinical Outcomes of Acute Ischemic Stroke Patients

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**KEYWORDS**

Stress Hyperglycemia; Fasting Blood Glucose–HbA1c Ratio; Acute Ischemic Stroke; Functional Independence; Clinical Outcome; Barthel Index

**ABSTRACT**

Stroke remains the second leading cause of mortality worldwide and the primary contributor to long-term disability. Stress hyperglycemia, calculated as the fasting blood glucose (FBG)–HbA1c ratio, has been proposed as a marker reflecting acute metabolic imbalance relative to chronic glycemic status, with potential prognostic value in acute ischemic stroke. This study aimed to evaluate the association between the FBG–HbA1c ratio and functional independence as well as clinical outcomes in acute ischemic stroke patients. A cross-sectional analytical observational study was conducted at Dr. Zainoel Abidin General Hospital. Consecutive sampling was utilized to recruit patients with acute ischemic stroke who fulfilled the inclusion criteria. The FBG–HbA1c ratio was calculated and analyzed in relation to functional independence using the Barthel Index (BI) and clinical outcome using the Modified Rankin Scale (mRS). The Pearson product-moment correlation test was used to determine the relationship between these variables. A total of 61 patients were included. The FBG–HbA1c ratio demonstrated a significant negative correlation with the Barthel Index ($R = -0.43$; $p = 0.04$) and a significant positive correlation with the mRS ($R = 0.508$; $p = 0.03$). The FBG–HbA1c ratio showed significant correlations with both functional independence and clinical outcomes, indicating its potential as a simple and reliable prognostic marker. A higher ratio reflects greater stress-induced hyperglycemia, which is associated with poorer neurological function and outcomes in acute ischemic stroke patients.

## INTRODUCTION

Stroke continues to represent a significant global health challenge, ranking as the second leading cause of mortality and the primary cause of long-term disability worldwide (GBD 2021 Stroke Collaborators, 2023; Feigin et al., 2021). According to the Global Burden of Disease (GBD) 2021 report, stroke accounted for more than seven million deaths, reflecting a 70% increase in incidence since 1990. The global economic burden exceeds US$890 billion annually---equivalent to approximately 0.66% of the world's GDP---and is projected to nearly double by 2050 (GBD 2021 Stroke Collaborators, 2023). This escalating burden underscores the urgent need to identify accurate prognostic markers that can improve clinical outcomes and functional recovery after stroke.

Hyperglycemia is a frequent metabolic disturbance observed during the acute phase of ischemic stroke and has been consistently linked to higher rates of mortality and disability (Kruyt et al., 2010; Fuentes et al., 2009). It can occur in both diabetic and non-diabetic patients as a component of the neuroendocrine stress response (Dungan et al., 2009). These stress hormones suppress insulin secretion, enhance hepatic glycogenolysis and gluconeogenesis, and consequently induce transient elevations in plasma glucose, a condition referred to as stress hyperglycemia. Approximately 8–35% patients with acute ischemic stroke develop stress-induced hyperglycemia, which has been linked to larger infarct volumes, hemorrhagic transformation, and worse neurological outcomes (Fuentes et al., 2009; Sung et al., 2017).

Over the past decade, a novel index known as the stress hyperglycemia ratio (SHR)---calculated as the ratio of fasting blood glucose (FBG) to glycated hemoglobin (HbA1c)---has been proposed to better quantify acute metabolic dysregulation relative to chronic glycemic status (Roberts et al., 2015). Roberts et al. (2015) first introduced this concept in critically ill patients, and subsequent studies demonstrated its prognostic value for predicting mortality and functional disability following acute ischemic stroke (Roberts et al., 2015; Krongsut & Kaewkrasaesin, 2024; Cai et al., 2022). Nevertheless, evidence remains inconsistent: some studies have shown a strong association between elevated FBG–HbA1c ratio and poor neurological outcomes, while others have reported nonsignificant or variable findings, particularly among diabetic populations (Pan et al., 2017). Moreover, most data derive from non-Asian cohorts, leaving a paucity of evidence regarding the prognostic role of this ratio among Southeast Asian populations.

Indonesia, a country with a high prevalence of diabetes and hypertension, faces a substantial stroke burden (Hussain et al., 2016). Despite the growing body of international evidence, research evaluating the association between the FBG-HbA1c ratio and functional independence as well as clinical outcomes in acute ischemic stroke within the Indonesian and broader Southeast Asian populations remains critically limited.

Therefore, this study aimed to assess the association between the FBG–HbA1c ratio, functional independence, and clinical outcomes in patients with acute ischemic stroke. The findings are expected to contribute to the development of a simple, cost-effective prognostic biomarker that is clinically relevant to stroke management in Indonesia and to strengthen the scientific foundation for metabolic optimization during the acute phase of stroke care.

## METHOD

This study is an analytical observational study with a cross-sectional approach. The study was carried out at Dr. Zainoel Abidin General Hospital, Aceh, Indonesia, from March to August 2025.

Patients diagnosed with acute ischemic stroke who were admitted to Dr. Zainoel Abidin General Hospital during the study period constituted the study population. Sampling was performed consecutively, including all eligible patients who fulfilled the inclusion criteria until the required number of subjects was reached. The sample size was determined using the numerical correlation formula with a 95% confidence level ($\alpha = 0.05$) and statistical power of 80% ($\beta = 0.20$). Based on the anticipated correlation coefficient (r) of 0.35 derived from previous literature and using the formula $n = [(Z\alpha + Z\beta)/C]^2 + 3$, where $C = 0.5 \times \ln[(1+r)/(1-r)]$, the minimum required sample size was calculated to be 61 participants.

Eligible participants were adults aged over 18 years with a confirmed diagnosis of acute ischemic stroke based on clinical examination and CT scan findings. FBG was measured using the enzymatic glucose oxidase method with a hexokinase assay on an automated biochemistry analyzer, while HbA1c was quantified using high-performance liquid chromatography (HPLC). Functional independence was assessed using the Barthel Index (BI), a standardized 10-item scale ranging from 0 to 100 that evaluates activities of daily living, with higher scores indicating greater independence. Clinical outcomes were measured using the Modified Rankin Scale (mRS), a 7-point ordinal scale (0-6) assessing global disability, where lower scores represent better functional outcomes. Patients were excluded if they presented with non-ischemic lesions on CT scan, reduced consciousness, or comorbidities that could interfere with glucose metabolism or hemoglobin measurements, such as chronic kidney disease, ongoing hemodialysis, erythropoietin therapy, or hematologic disorders including hemoglobinopathies, anemia, or thalassemia.

Demographic, clinical, and laboratory data were obtained from hospital medical records. The collected variables included age, gender, and risk factors such as hypertension, diabetes mellitus, dyslipidemia, and hyperuricemia. Laboratory parameters included FBG and HbA1c levels measured upon admission using standardized laboratory procedures. The FBG–HbA1c ratio, reflecting acute metabolic stress relative to chronic glycemic status, was calculated for each participant by dividing the FBG value (mmol/L), by the corresponding HbA1c percentage. Functional independence was assessed using the BI, while overall clinical outcome was evaluated with the mRS at the end of hospitalization. All laboratory examinations were performed in the hospital's central clinical laboratory under standard operational protocols.

Statistical analysis was carried out using IBM SPSS Statistics for Windows, Version 26.0. Relationships between the FBG–HbA1c ratio and functional outcomes were determined using either the Pearson product–moment correlation or the Spearman rank correlation method, depending on data distribution. A 95% confidence level was used, and results with p-values below 0.05 were regarded as statistically significant.

This study was approved by the Ethics Committee of Dr. Zainoel Abidin General Hospital, Banda Aceh, Indonesia (Approval No. 036/ETIK-RSUDZA/2025).

## RESULT AND DISCUSSION

### Characteristics of research subjects

A total of 61 patients with acute ischemic stroke were enrolled in this study. The median age of the participants was 59 years (range: 19–71 years). The majority of patients were male (62.3%), while female patients accounted for 37.7%. The most frequent vascular risk factor was hypertension, present in 60.7% of the subjects, followed by diabetes mellitus in 59%, dyslipidemia in 44.3%, and hyperuricemia in 16.4% (Table 1).

**Table 1. Subject characteristics**

| Characteristics | Mean / Frequency |
|---|---|
| Age (years), median (min – max) | 59 (19 – 71) |
| Gender, n (%) | |
| Male | 38 (62.3) |
| Female | 23 (37.7) |
| **hypertension**, n (%) | 37 (60.7) |

| | |
|---|---|
| Diabetes mellitus, n (%) | 36 (59) |
| **Dyslipidemia**, n (%) | 27 (44.3) |
| **Hyperuricemia**, n (%) | 10 (16.4) |

**FBG–HbA1c ratio and functional independence**

The mean FBG–HbA1c ratio among participants was 0.95 ± 0.28, while the mean BI score was 65.4 ± 24.2. Correlation analysis using the Pearson Product Moment test demonstrated a significant negative correlation between the FBG–HbA1c ratio and the BI (r = –0.43, p = 0.04) (Table 2). The scatter plot illustrated in Figure 1 demonstrates a downward distribution pattern from left to right, accompanied by a regression trend line consistently showing a negative slope, further reinforcing the presence of a negative correlation between the two variables. Accordingly, patients with higher FBG–HbA1c ratios tend to have lower BI scores, emphasizing the role of glucose metabolic disturbance in reducing functional independence.

**Table 2. Analysis of the relationship between the FBG–HbA1c Ratio and the BI**

| | Mean ± SD | r | p-value* |
|---|---|---|---|
| FBG-HbA1c | 0.95 ± 0.28 | -0.43 | 0.04 |
| BI | 65.4 ± 24.2 | | |

* Pearson's correlation test

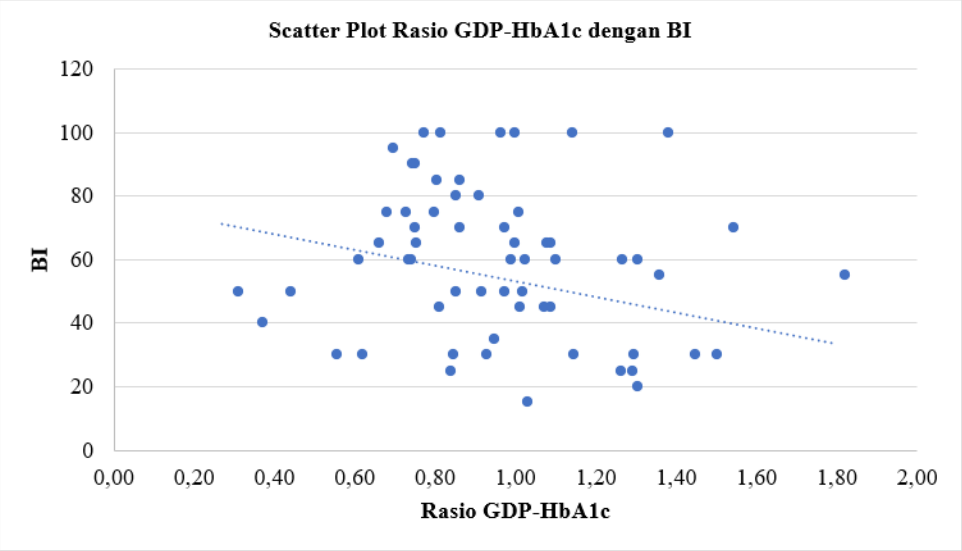


Figure 1. Scatter plot illustrating the relationship between the FBG–HbA1c ratio and the BI

FBG–HbA1c ratio and clinical outcomes

The median score of the mRS was 2 (range: 1–4), indicating mild to moderate disability among the majority of patients. The FBG–HbA1c ratio showed a significant positive correlation with mRS scores (r = 0.508, p= 0.03) (Table 3), suggesting that a higher ratio was associated with poorer clinical outcomes. The data distribution visualized in Figure 2 shows a scatter plot with an upward trend corresponding to the increase in the FBG–HbA1c ratio, while the ascending regression trend line further supports the presence of a positive correlation between the two variables. Accordingly, this finding indicates that a higher degree of acute

dysglycemia is associated with more severe functional outcomes in patients with acute ischemic stroke.

**Table 3. Analysis of the relationship between the FBG–HbA1c Ratio and the mRS**

| | Median | Min – Max | r | p-value* |
|---|---|---|---|---|
| GDP-HbA1c ratio | 0.95 | 0.31 – 1.82 | 0.508 | 0.03 |
| mRS | 2 | 1 – 4 | | |

* Spearman's correlation test

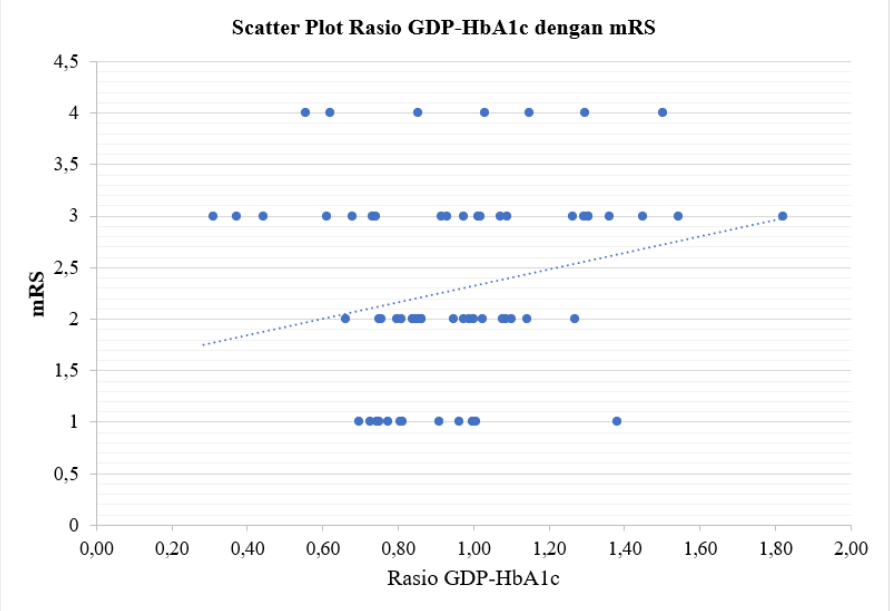


Figure 2. Scatter plot illustrating the relationship between the FBG–HbA1c ratio and the mRS

## Discussion

In this study, the characteristics of the participant reflect a combination of interrelated risk factors, encompassing both non-modifiable and controllable factors. Age represents the strongest non-modifiable risk factor, as the majority of stroke cases occur after the age of 55–60 years, with both incidence and severity increasing progressively with advancing age (Feigin et al., 2018). In terms of sex distribution, male patients predominated (62.3%) compared to females (37.7%). This finding is consistent with the report by Fatima et al. (2020), which demonstrated a higher incidence of stroke among men of productive age. However, in women, the risk increases after menopause due to the loss of estrogen's protective effects and their relatively longer life expectancy compared to men (Fatima et al., 2020; Appelros et al., 2009).

Diabetic patients tend to experience stroke at a younger age and often present with a greater burden of comorbidities. This risk increases with longer disease duration, as reported by Boehme et al. (2017). Other metabolic factors, such as dyslipidemia---characterized by elevated cholesterol levels, particularly LDL---contribute to the acceleration of atherosclerosis and further increase the risk of stroke, especially when accompanied by hypertension, diabetes, or hyperuricemia (Boehme et al., 2017).

Hypertension remains the most significant modifiable risk factor, as chronic high blood pressure induces progressive vascular damage and accelerates atherosclerosis, making its control essential for both primary and secondary prevention. Additionally, hyperuricemia has

recently been recognized as an independent risk factor of incidence, severity, and mortality of stroke, particularly among postmenopausal women, through mechanisms involving oxidative stress, endothelial dysfunction, atherosclerosis, and platelet aggregation. Overall, these findings emphasize that acute ischemic stroke is not solely influenced by demographic factors such as age and gender, but is also strongly associated with metabolic factors including diabetes, dyslipidemia, hypertension, and hyperuricemia (Fatima et al., 2020; Appelros et al., 2009; Boehme et al., 2017).

This study demonstrated that the FBG–HbA1c ratio, an indicator of stress hyperglycemia, was significantly correlated with functional outcomes in patients with acute ischemic stroke. Specifically, a higher FBG–HbA1c ratio was associated with lower BI scores and higher mRS scores, indicating decreased functional independence and worse neurological outcomes. The results of this study are consistent with prior evidence showing that hyperglycemia during the acute phase of stroke adversely affects neurological recovery. Cai et al. (2022) reported that a higher FBG to HbA1c ratio was associated with an increased risk of all-cause mortality and functional disability in stroke patients. Similarly, Krongsut and Kaewkrasaesin (2024) demonstrated that the FBG–HbA1c ratio was an significant predictor of fatal outcomes in patients with thrombolyzed acute ischemic stroke. Habibur et al. (2022) further confirmed that elevated HbA1c levels and high stress hyperglycemia ratios were associated with poorer outcomes, particularly in patients with diabetes mellitus. These studies support the current findings, reinforcing the clinical value of the FBG–HbA1c ratio as a prognostic tool that integrates acute metabolic stress with baseline glycemic control.

When compared to regional studies, our findings align with recent research from neighboring Southeast Asian countries. A study by Nguyen et al. (2023) in Vietnam reported similar associations between stress hyperglycemia and poor functional outcomes in acute stroke patients, with comparable effect sizes. However, their cohort showed a lower prevalence of diabetes mellitus (42%) compared to our study population (59%), potentially reflecting differences in regional metabolic profiles. In a Malaysian multicenter study by Ahmad et al. (2022), the FBG-HbA1c ratio demonstrated even stronger predictive value (AUC = 0.78) for 3-month mortality compared to conventional glucose measurements alone, supporting the clinical utility of this marker in diverse Southeast Asian populations. Notably, these regional studies consistently report higher baseline HbA1c levels and more severe metabolic dysregulation in Southeast Asian stroke patients compared to Western cohorts, suggesting that ethnicity-specific metabolic factors may influence stroke outcomes and warrant population-tailored management strategies.

The observed correlation between a higher FBG–HbA1c ratio and worse stroke outcomes may be explained by several biological mechanisms. Acute hyperglycemia can exacerbate ischemic brain injury through multiple pathways, including oxidative stress, endothelial dysfunction, increased blood–brain barrier permeability, and inflammatory activation (Martini & Kent, 2007; Capes et al., 2001; Bruno et al., 1999). The surge of counterregulatory hormones such as cortisol and catecholamines during the stress response enhances gluconeogenesis and glycogenolysis, resulting in elevated circulating glucose levels (Marik & Bellomo, 2013). In turn, this metabolic disturbance promotes excessive production of reactive oxygen species (ROS), leading to neuronal apoptosis and expansion of the infarct area (Capes et al., 2001). Moreover, chronic hyperglycemia, reflected by elevated HbA1c, contributes to the formation

of advanced glycation end products (AGEs), vascular inflammation, and atherosclerotic progression, all of which impair cerebrovascular autoregulation and limit recovery potential after ischemic injury (Singh et al., 2001). Thus, the FBG–HbA1c ratio provides a dynamic reflection of both acute and chronic metabolic states, and its elevation likely represents the combined effect of poor long-term glycemic control and heightened stress-induced glucose dysregulation during the acute event (Cai et al., 2022).

Although most previous studies have reported similar associations between stress hyperglycemia and poor functional outcomes, some discrepancies exist in the strength of correlation or statistical significance. For instance, Sung et al. (2017) found that FBG was a more reliable predictor of neurological outcome than random glucose or HbA1c alone, but the prognostic superiority of the FBG–HbA1c ratio was not uniformly observed across all patient groups. Differences in population characteristics, such as the proportion of diabetic versus non-diabetic patients, the severity of stroke, and treatment modalities including thrombolysis or thrombectomy, may explain the variations in results among studies (Cai et al., 2022). Furthermore, ethnic and regional differences may influence metabolic responses and stroke outcomes (Nguyen et al., 2023; Ahmad et al., 2022; Kim et al., 2014; Foo & Lo, 2019). Most prior research on stress hyperglycemia ratios has been conducted in East Asian or Western populations, whereas data from Southeast Asia, including Indonesia, remain limited.

This study's findings contribute new evidence from an Indonesian cohort, where the prevalence of diabetes, hypertension, and dyslipidemia is high (Hussain et al., 2016). These comorbidities likely exacerbate the adverse effects of stress-induced hyperglycemia by amplifying systemic inflammation and endothelial dysfunction, thereby worsening stroke prognosis (Cai et al., 2022). The distinct metabolic and genetic profile of the Indonesian population, characterized by higher rates of carbohydrate-rich diets and earlier onset of metabolic syndrome, may further contribute to the pronounced association between the FBG-HbA1c ratio and poor outcomes observed in this study.

The clinical implications of these findings are substantial. The FBG–HbA1c ratio represents an easily obtainable, cost-effective laboratory parameter that can be incorporated into the early assessment of patients with acute ischemic stroke. Because both fasting glucose and HbA1c are routinely measured upon hospital admission, calculating their ratio requires no additional cost or specialized equipment. Integrating this index into clinical risk stratification models may help identify patients at higher risk of poor recovery, allowing for timely interventions such as stricter glycemic monitoring, optimized metabolic control, and individualized rehabilitation strategies.

This study has several limitations. First, the cross-sectional design prevents the determination of a causal relationship between the FBG–HbA1c ratio and functional outcomes. Second, the relatively small sample size and single-center setting may restrict the generalizability of the findings to broader populations. Third, follow-up data beyond the acute hospitalization period were not available, preventing assessment of long-term outcomes. Finally, potential confounders such as nutritional status, infection, and unmeasured metabolic factors might have influenced glucose variability and clinical recovery. Future multicenter, longitudinal studies with larger sample sizes are warranted to validate these findings and determine whether interventions targeting stress hyperglycemia can improve post-stroke outcomes.

## CONCLUSION

This study found a significant association between the FBG–HbA1c ratio and functional independence as well as clinical outcomes in patients with acute ischemic stroke. A higher FBG–HbA1c ratio, representing greater stress-induced hyperglycemia, was correlated with lower BI scores and higher mRS scores, indicating reduced functional independence and poorer neurological outcomes. These findings highlight the FBG–HbA1c ratio as a simple, practical, and cost-effective biomarker that integrates acute and chronic glycemic states, enabling early risk stratification and prognostic assessment in acute stroke care. Further multicenter and longitudinal studies are needed to validate these findings and determine whether interventions targeting stress hyperglycemia can improve recovery and long-term outcomes.

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