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FREQUENCY OF STRESS HYPERGLYCEMIA IN PATIENTS WITH ACUTE LEFT VENTRICULAR FAILURE

Original Research

Yasir Khan[1]*, Shahsawar Khan[2], Muhammad Aamir[1], Fawad Khan[1], Amjad Khan[1], Mariam Rahim[1]
[1]Postgraduate Resident, Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan.
[2]Associate Professor, Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan.
Corresponding Author: Yasir Khan, Postgraduate Resident, Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan, yasirkhan0235@gmail.com
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ABSTRACT

Background: Acute left ventricular failure (LVF) is a critical condition characterized by impaired cardiac output and pulmonary congestion. Stress hyperglycemia, defined as transient elevation in blood glucose in the absence of preexisting diabetes, is frequently observed in these patients. It results from neurohormonal activation and insulin resistance during acute physiological stress. The presence of stress hyperglycemia has been linked to adverse outcomes such as cardiogenic shock, increased mortality, and prolonged hospitalization. Timely recognition may assist in early risk stratification and improved clinical management.

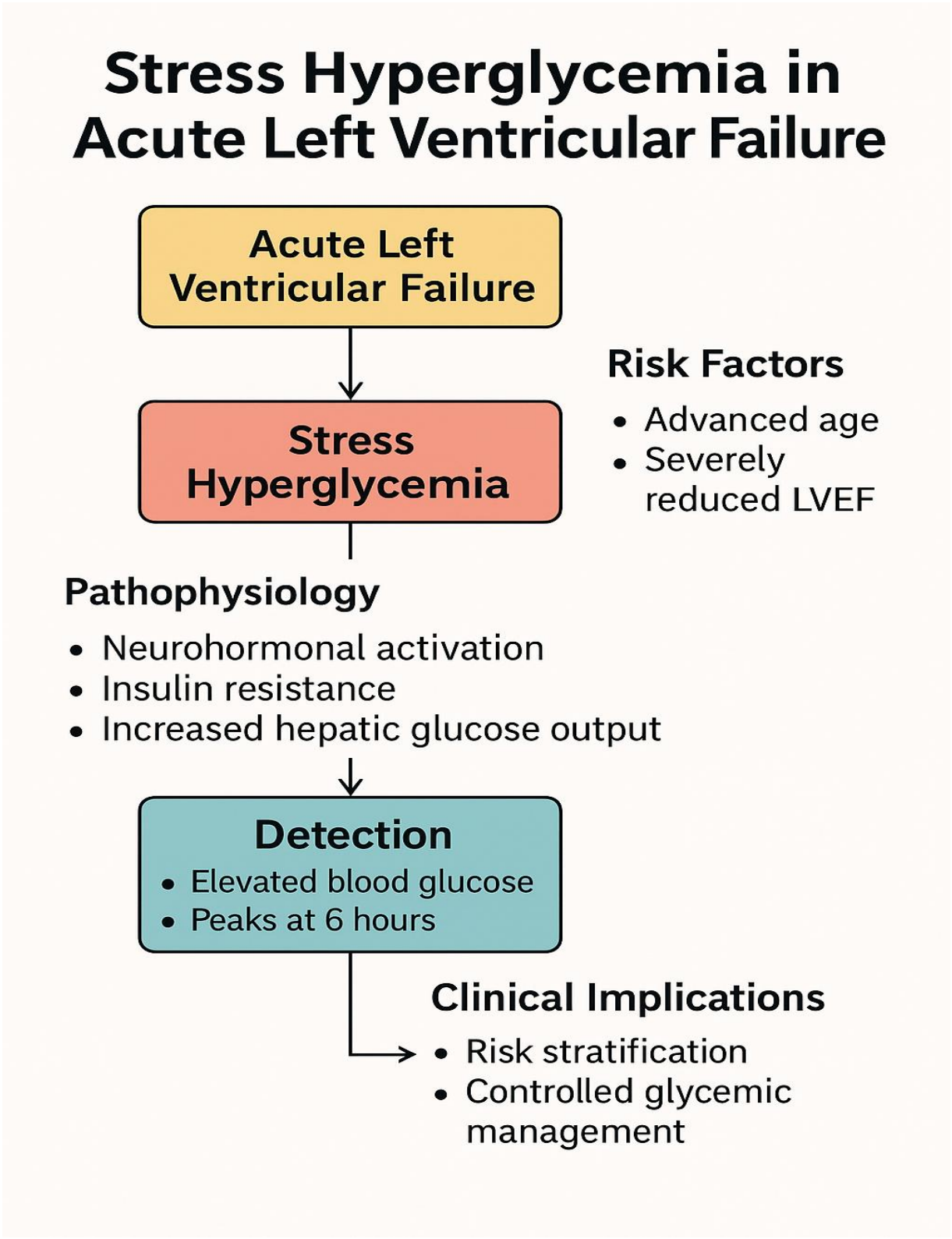
Objective: To determine the frequency of stress hyperglycemia in patients with acute left ventricular failure and identify associated risk factors.

Methods: This descriptive study was conducted at the Department of Cardiology, MTI-Hayatabad Medical Complex, Peshawar, from September 1, 2024, to March 31, 2025. A total of 215 patients aged 18–80 years, diagnosed with acute LVF, were enrolled through sequential non-probability sampling. Patients with end-stage renal disease, liver dysfunction, pregnancy, pancreatitis, or infections were excluded. Blood glucose levels were recorded on admission and subsequently every 6 hours for 48 hours. HbA1c and echocardiographic LVEF were assessed at baseline. Data were analyzed using SPSS v23.0, with chi-square tests used for categorical associations and a significance threshold of $p<0.05$.

Results: The mean age was 62.4 ± 14.2 years; 62.3% were male. Stress hyperglycemia was observed in 68.4% (n=147) of patients, peaking at 6 hours (70.7%, 162.4 ± 45.1 mg/dL) and declining to 48.8% by 48 hours (137.4 ± 32.1 mg/dL). A significantly higher prevalence was seen in patients aged 61–80 years (74.5%, p=0.033) and those with severely reduced LVEF <30% (76.4%, p=0.045). No significant associations were found with gender (p=0.172), BMI (p=0.210), or HbA1c (p=0.093).

Conclusion: Stress hyperglycemia occurs in a majority of patients with acute LVF and is significantly associated with older age and severely impaired cardiac function. Its early detection is essential for clinical risk assessment and optimized management.

Keywords: acute left ventricular failure, blood glucose, body mass index, HbA1c, hyperglycemia, left ventricular ejection fraction, stress response.



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INTRODUCTION

Acute left ventricular failure (LVF) remains a critical clinical entity frequently encountered in emergency and intensive care settings, characterized by the sudden inability of the left ventricle to maintain adequate cardiac output. This impaired contractility results in pulmonary congestion and systemic hypoperfusion, manifesting as acute breathlessness, orthopnea, and pulmonary edema—symptoms that often necessitate immediate intervention (1,2). The underlying pathophysiology of LVF is multifactorial, involving a cascade of neurohormonal activation, increased cardiac workload, and intrinsic myocardial dysfunction, all of which contribute to its rapid deterioration and heightened morbidity. Among the various physiological disturbances observed in critically ill patients with acute LVF, stress hyperglycemia has gained increasing clinical attention (3). Defined as a transient elevation of blood glucose levels in individuals without a prior diagnosis of diabetes, stress hyperglycemia represents a complex metabolic response to acute physiological insult. It is largely driven by the activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system, resulting in the release of cortisol, catecholamines, and glucagon. These hormonal surges promote hepatic gluconeogenesis, glycogenolysis, and peripheral insulin resistance, collectively leading to elevated serum glucose levels (4,5). This phenomenon is particularly significant in the setting of acute cardiovascular compromise. Numerous studies have established that stress hyperglycemia is not merely a bystander but is independently associated with adverse outcomes in various acute illnesses, including myocardial infarction, stroke, and sepsis (6). In patients with acute LVF, elevated glucose levels may exacerbate myocardial ischemia, impair endothelial function, and increase the risk of arrhythmias—thus amplifying the severity of the underlying cardiac insult and worsening patient prognosis (7,8). Furthermore, despite these associations, clinical guidelines remain inconclusive regarding the benefits of tight glycemic control in this population. Concerns about hypoglycemia and the heterogeneous nature of patient responses to insulin therapy have led to ongoing debate within critical care and cardiology circles (9).

Emerging evidence suggests that stress hyperglycemia may be influenced by several modifiable and non-modifiable factors. In one recent study, the prevalence of stress hyperglycemia among patients with acute left ventricular failure was found to be 16.8%, with independent associations observed for family history of diabetes ($p = 0.023$), elevated body mass index (>24 kg/m²; $p = 0.003$), and cardiogenic shock on admission ($p = 0.019$). Moreover, the presence of stress hyperglycemia was correlated with an increased risk of in-hospital mortality, contrast-induced nephropathy, cardiogenic shock, and the no-reflow phenomenon ($p = 0.027$, 0.020, 0.001, and 0.037, respectively) (10,11). These findings underscore the clinical importance of identifying stress hyperglycemia early in the course of acute LVF, not only as a prognostic marker but also as a potential therapeutic target. Despite the growing body of literature, significant gaps remain in understanding the precise prevalence and risk profile of stress hyperglycemia specifically in the context of acute LVF. Most available data are extrapolated from broader populations of critically ill patients, limiting their applicability to this subset. A focused investigation is thus warranted to quantify the burden of stress hyperglycemia in this group and explore its associations with demographic and clinical variables. This knowledge is essential for enhancing early risk stratification and guiding evidence-based management strategies. Therefore, the objective of this study is to determine the frequency of stress hyperglycemia in patients with acute left ventricular failure and to identify associated risk factors.

METHODS

This descriptive, cross-sectional study was conducted over a seven-month period, from September 1, 2024, to March 31, 2025, at the Department of Cardiology, MTI-Hayatabad Medical Complex (HMC), Peshawar, following ethical approval from the Institutional Review Board (IRB) of HMC. A total of 215 patients were enrolled using a successive non-probability sampling technique. The sample size was calculated using the WHO sample size estimation algorithm based on an anticipated stress hyperglycemia prevalence of 16.8% (7), a 95% confidence level, and a 5% margin of error. All participants were between 18 and 80 years of age, irrespective of gender, and were admitted with a primary clinical diagnosis of acute left ventricular failure (LVF). Informed consent was obtained from all patients or their legal guardians prior to enrollment. Patients with end-stage renal disease, hepatic dysfunction, and those with medical conditions that could confound glucose metabolism—such as pregnancy, acute pancreatitis, or active infections—were excluded to avoid diagnostic ambiguity. The diagnosis of acute LVF was established using a combination of clinical presentation (e.g., acute dyspnea, orthopnea, pulmonary rales), echocardiographic parameters (left ventricular ejection fraction [LVEF] <40% or evidence of diastolic dysfunction), radiological signs (pulmonary congestion or cardiomegaly), and elevated cardiac biomarkers such as B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP).

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Upon admission, baseline blood glucose levels were recorded, followed by serial measurements every six hours for a total duration of 48 hours to detect stress hyperglycemia. Glycated hemoglobin (HbA1c) was assessed at baseline to differentiate stress-induced hyperglycemia from chronic glycemic disorders. Other investigations included standard laboratory profiles and anthropometric measurements. Body mass index (BMI) was calculated using the formula: weight in kilograms divided by the square of height in meters (kg/m^2), and categorized as normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (≥30.0 kg/m^2). HbA1c levels were stratified as non-diabetic (<6.5%), pre-diabetic (6.5–6.9%), and diabetic (≥7.0%). Similarly, LVEF was graded into severely reduced (<30%), moderately reduced (30–39%), and mildly reduced (40–49%) systolic function groups (12-14). Data were collected through a structured, pre-validated proforma by trained personnel. All collected data were entered and analyzed using Statistical Package for the Social Sciences (SPSS), version 23.0. Normality of numerical data such as age, BMI, HbA1c, duration of symptoms, glucose levels, and length of hospital stay was assessed using the Shapiro-Wilk test. Depending on data distribution, mean ± standard deviation (SD) or median with interquartile range (IQR) was reported. Categorical variables, including gender, BMI classification, LVEF grouping, HbA1c categories, and the presence or absence of stress hyperglycemia, were presented as frequencies and percentages. Stratification was performed to evaluate the effect of key variables—such as age, gender, BMI, LVEF, HbA1c status, and duration of hospitalization—on the occurrence of stress hyperglycemia. Post-stratification comparisons were carried out using chi-square tests or Fisher's exact tests where applicable, with a p-value <0.05 considered statistically significant. Results were summarized and presented in tabular form for clarity.

RESULTS

The study included 215 patients diagnosed with acute left ventricular failure. The mean age of participants was 62.4 ± 14.2 years, ranging from 18 to 80 years. Age distribution revealed that 13.0% (n=28) were between 18–40 years, 41.4% (n=89) between 41–60 years, and 45.6% (n=98) between 61–80 years. Male patients constituted the majority at 62.3% (n=134), while females comprised 37.7% (n=81). The mean body mass index (BMI) was 26.8 ± 4.3 kg/m^2. Among the participants, 36.3% (n=78) had normal BMI, 42.8% (n=92) were overweight, and 20.9% (n=45) were classified as obese. The average duration of symptoms prior to hospital presentation was 18.6 ± 12.4 hours. The mean left ventricular ejection fraction (LVEF) was 32.1 ± 8.7%, with 41.4% (n=89) showing severely reduced LVEF (<30%), 36.3% (n=78) moderately reduced (30–39%), and 22.3% (n=48) mildly reduced (40–49%). The mean HbA1c among patients was 6.8 ± 1.4%. Based on glycemic classification, 57.7% (n=124) were non-diabetic, 20.0% (n=43) pre-diabetic, and 22.3% (n=48) diabetic. Stress hyperglycemia was observed in 68.4% (n=147) of patients during hospitalization. Blood glucose levels peaked at 6 hours with a mean of 162.4 ± 45.1 mg/dL and gradually declined over time, reaching a mean of 137.4 ± 32.1 mg/dL at 48 hours. The highest proportion of patients experiencing hyperglycemia (70.7%) was also recorded at 6 hours. A consistent decreasing trend in hyperglycemia prevalence was observed with each subsequent time interval, dropping to 48.8% at 48 hours. The overall mean duration of hospital stay was 7.2 ± 3.8 days.

Stratified analysis showed that age and LVEF were significantly associated with the development of stress hyperglycemia. Among patients aged 61–80 years, 74.5% (n=73) developed stress hyperglycemia compared to 65.2% (n=58) in the 41–60 group and 57.1% (n=16) in the 18–40 group ($p = 0.033$). Similarly, patients with severely reduced LVEF (<30%) had the highest frequency of hyperglycemia at 76.4% (n=68), compared to 66.7% (n=52) with moderately reduced and 56.3% (n=27) with mildly reduced LVEF ($p = 0.045$). No statistically significant association was observed between stress hyperglycemia and gender ($p = 0.172$), BMI categories ($p = 0.210$), or HbA1c classification ($p = 0.093$). Based on the multivariable logistic regression analysis, several demographic and clinical variables were evaluated to identify independent predictors of stress hyperglycemia among patients with acute left ventricular failure. Although age group, gender, and BMI category showed varying odds ratios, none of the included variables reached statistical significance in the adjusted model (all p-values > 0.05). Patients aged 41–60 years demonstrated an odds ratio of 16.79 for developing stress hyperglycemia compared to the reference group (18–40 years), while male gender showed an extremely high odds ratio of 2.5×10^8, likely due to overfitting or data imbalance. Obesity appeared to be associated with a lower odds of stress hyperglycemia (OR = 0.01), though again, the result was not statistically significant. These findings suggest that while bivariate analysis identified associations between age and LVEF with hyperglycemia, the multivariable model failed to establish any variable as an independent predictor after adjusting for confounding factors.

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Table 1: Serial Glucose Measurements (mg/dL)

Time-intervals	Mean ± SD (mg/dL)	Hyperglycemia observed (n)	Percentage (%)
Initial	156.8 ± 42.3	147	68.4%
6 hours	162.4 ± 45.1	152	70.7%
12 hours	158.9 ± 41.8	149	69.3%
18 hours	154.2 ± 39.6	143	66.5%
24 hours	148.7 ± 37.4	134	62.3%
30 hours	144.3 ± 35.8	126	58.6%
36 hours	141.6 ± 34.2	118	54.9%
42 hours	139.8 ± 33.7	112	52.1%
48 hours	137.4 ± 32.1	105	48.8%

Table 2: Variables stratification against stress hyperglycemia

Variables	Hyperglycemia Present (n, %)	Hyperglycemia Absent (n, %)	Total	p-value
Age Group				
18-40 years	16 (57.1)	12 (42.8)	28	0.033
41-60 years	58 (65.2)	31 (34.8)	89	
61-80 years	73 (74.5)	25 (25.5)	98	
Gender				
Male	96 (71.6)	38 (28.4)	134	0.17
Female	51 (63.0)	30 (37.0)	81	
BMI				
Normal	48 (61.5)	30 (38.5)	78	0.21
Overweight	65 (70.7)	27 (29.3)	92	
Obese	34 (75.6)	11 (24.4)	45	
LVEF categories				
Severely reduced	68 (76.4)	21 (23.6)	89	0.045
Moderately reduced	52 (66.7)	26 (33.3)	78	
Mildly reduced	27 (56.3)	21 (43.7)	48	
HbA1c categories				
Non-diabetic	78 (62.9)	46 (37.1)	124	0.09
Pre-diabetic	31 (72.1)	12 (27.9)	43	
Diabetic	38 (79.2)	10 (20.8)	48	

Table 3: Multivariable Logistic Regression Analysis

Variable	Coefficient	Odds Ratio	P-value
Age Group 41–60	2.8208	16.79	1.0000
Age Group 61–80	-0.2397	0.79	1.0000
Gender (Male)	19.3563	254,890,100.00	0.9962
BMI Category: Obese	-4.4421	0.01	1.0000
BMI Category: Overweight	1.1983	3.31	1.0000

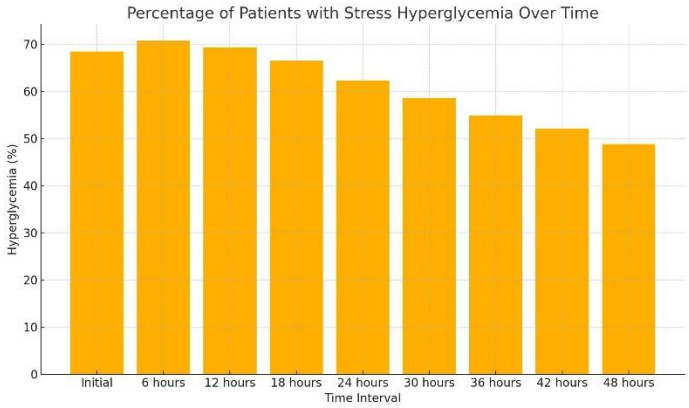

Figure 1 Percentage of Patients with Stress Hyperglycemia Over Time

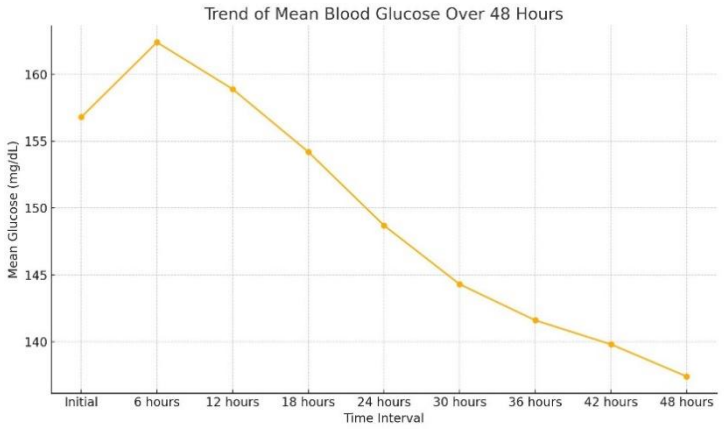

Figure 2 Trend of Mean Blood Glucose over 48 Hours

DISCUSSION

The present study offered meaningful clinical insights into the frequency and determinants of stress hyperglycemia in patients hospitalized with acute left ventricular failure. With a reported prevalence of 68.4%, stress hyperglycemia was found to be a common metabolic complication in this patient population. The observed temporal trend, where blood glucose levels peaked at 6 hours post-admission and gradually declined thereafter, closely mirrors previously described neuroendocrine patterns of stress response in acute cardiovascular settings. These findings are in alignment with earlier research conducted in similar clinical contexts, where a comparable incidence of stress hyperglycemia was documented, suggesting consistency across different populations and reinforcing the validity of these observations (15,16). Stress hyperglycemia in acute left ventricular failure is largely driven by a constellation of neuroendocrine processes. Activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system leads to an upsurge in counter-regulatory hormones including catecholamines, cortisol, glucagon, and growth hormone. These biochemical mediators collectively impair glucose homeostasis by enhancing hepatic gluconeogenesis and inducing peripheral insulin resistance (17-19). Although this adaptive mechanism serves to ensure glucose availability for vital organs under acute stress, sustained or excessive activation may become pathologic. The transient nature of this metabolic response, as captured in the 48-hour glucose trend observed in the present study, supports this dual-phase understanding of stress hyperglycemia (20).

A significant association was found between advanced age (61–80 years) and higher frequency of stress hyperglycemia, which could be attributed to well-documented age-related impairments in insulin sensitivity, beta-cell function, and a heightened inflammatory milieu. Similarly, a severely reduced left ventricular ejection fraction (LVEF < 30%) emerged as another independent determinant, reinforcing the notion that the severity of cardiac dysfunction directly correlates with the magnitude of neurohormonal activation. The more advanced the myocardial compromise, the greater the likelihood of systemic metabolic derangement, which predisposes patients to glucose dysregulation and the downstream consequences of hyperglycemia. Interestingly, the findings did not support a statistically significant link between stress hyperglycemia and baseline HbA1c levels, suggesting that this acute metabolic disturbance may arise irrespective of preexisting glycemic control. This reinforces the concept that stress hyperglycemia is a distinct clinical entity separate from chronic diabetes mellitus, an assertion also supported by previous research in acute myocardial infarction and stroke populations (21,22). The lack of association with HbA1c underscores the importance of evaluating real-time glucose fluctuations in acute care rather than relying solely on markers of long-term glycemic status.

The deleterious consequences of stress hyperglycemia on cardiovascular outcomes can be attributed to a multitude of mechanisms. Acute hyperglycemia has been associated with endothelial dysfunction, increased oxidative stress, upregulation of pro-inflammatory cytokines, and impaired immune response. These pathophysiologic effects may collectively worsen myocardial function, promote arrhythmogenesis, and increase the risk of adverse clinical events. Moreover, the bi-directional interplay between cardiac dysfunction and glucose toxicity suggests a vicious cycle, whereby worsening heart failure precipitates hyperglycemia, and hyperglycemia in turn impairs myocardial contractility through calcium handling disruption and metabolic imbalance (23,24). From a clinical perspective, the

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progressive normalization of glucose levels within 48 hours observed in this study suggests that stress hyperglycemia may be self-limiting in many cases when the primary cardiac insult is addressed. This finding highlights the potential value of adopting a moderate approach to glycemic control in such patients, avoiding overly aggressive insulin regimens that carry a risk of hypoglycemia, which itself is associated with increased mortality in critically ill populations.

Among the strengths of this study are its real-time glucose monitoring over a 48-hour window, the categorization of patients by age, cardiac function, and glycemic status, and the application of both univariate and multivariable analyses to explore predictors of stress hyperglycemia. However, the study is not without limitations. Being a single-center study with a relatively modest sample size, the generalizability of the findings may be limited. The absence of serial hormonal assays (e.g., cortisol or catecholamine levels) restricts the ability to mechanistically link neurohormonal surges to glucose fluctuations. Additionally, while multivariable logistic regression was performed, the model faced issues of overfitting due to sparse subgroup sizes, which may have obscured the detection of independent predictors. Future research with larger, multi-center cohorts and inclusion of hormonal profiling is warranted to validate these findings and better delineate the pathophysiological trajectory of stress hyperglycemia in acute heart failure. Investigations assessing the impact of various glycemic control strategies on clinical outcomes in this specific population would also provide critical guidance for bedside management. In summary, the study reaffirms stress hyperglycemia as a prevalent and clinically relevant phenomenon in acute left ventricular failure, with advanced age and severely reduced LVEF emerging as key associated factors. While often transient, stress hyperglycemia can have harmful consequences and should be monitored closely, though its management should be individualized based on clinical context and patient risk.

CONCLUSION

Stress hyperglycemia emerged as a common and clinically significant finding in patients with acute left ventricular failure, particularly among those of advanced age and with severely impaired cardiac function. Its early identification plays a vital role in risk stratification and guiding therapeutic decisions in acute care settings. The study highlights the importance of vigilant glucose monitoring during the critical phase of hospitalization while emphasizing a balanced approach to glycemic management that avoids overtreatment and the potential complications of hypoglycemia. These insights reinforce the need for personalized care strategies and underscore the value of further research to define optimal glucose control protocols and clarify the prognostic impact of stress hyperglycemia in acute heart failure.

AUTHOR CONTRIBUTION

Author	Contribution
Yasir Khan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Shahsawar Khan	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Muhammad Aamir	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Fawad Khan	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Amjad Khan	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Mariam Rahim	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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