ARTICLE

Glycemic Variability and Its Outcome in Intensive Care Unit Patients with Sepsis in a Tertiary Care Centre, Puducherry

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ABSTRACT

Background: Sepsis-induced metabolic dysregulation produces pronounced fluctuations in blood glucose that persist even in the absence of chronic diabetes. While absolute hyperglycaemia has historically guided glycaemic management in intensive care, emerging evidence suggests that glycemic variability (GV)—the degree of oscillation in blood glucose over time—may independently predict adverse outcomes in critically ill patients. Data from Indian tertiary care settings remain limited.

Objective: To evaluate glycemic variability using the coefficient of variation (CV) of blood glucose and to determine its association with ICU mortality, length of ICU stay (LOS), organ support requirements, and final hospital outcome in sepsis patients admitted to a tertiary care ICU in Puducherry.

Methods: Prospective observational single-centre cohort study, seventy-two ICU patients fulfilling at least two sepsis criteria (Surviving Sepsis Campaign Guidelines 2026) were enrolled between April and June 2026. Capillary or venous blood glucose was recorded every 6 hours for the first 72 hours of ICU admission. Glycemic variability was quantified as CV (%) = (SD / Mean BG) × 100. Patients were stratified as High GV (CV ≥ 36%) or Low GV (CV < 36%). Clinical outcomes were recorded at ICU or hospital discharge. Statistical analysis employed independent samples t-test, chi-square test, Fisher's exact test, and Pearson correlation using SPSS v23.0.

Results: Of 72 patients (mean age 54.4 ± 15.1 years; 56.9% male; 58.3% diabetic), 26 (36.1%) had High GV and 46 (63.9%) had Low GV. ICU mortality was significantly higher in the High GV group (42.3% vs 4.3%; $p < 0.001$). Mean ICU LOS was prolonged in High GV patients (13.0 ± 4.2 vs 9.6 ± 3.4 days; $p = 0.001$). Multiple organ dysfunction syndrome (MODS) occurred significantly more in the High GV group (57.7% vs 30.4%; $p = 0.023$). A significant positive correlation was demonstrated between CV and ICU LOS (Pearson $r = 0.42$, $p < 0.001$). APACHE II and SOFA Day 1 scores were significantly higher in the High GV group ($p < 0.05$). All nine episodes of hypoglycaemia occurred exclusively within the High GV group.

Conclusion: High glycemic variability (CV ≥ 36%), as measured from routine bedside glucose monitoring, is a clinically significant and statistically robust predictor of ICU mortality, prolonged stay, and greater illness severity in patients with sepsis. Integration of GV metrics into routine ICU glycaemic assessment protocols may enhance risk stratification and guide targeted glucose management strategies in resource-limited settings.

Keywords: Glycemic variability, coefficient of variation, sepsis, intensive care unit, mortality, length of stay, APACHE II, SOFA

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INTRODUCTION

Sepsis remains one of the foremost causes of mortality in intensive care units (ICUs) worldwide, accounting for over 11 million deaths annually and representing an estimated 20% of all global deaths.(1,2) Patients with sepsis exhibit profound perturbations in metabolic homeostasis, among which dysregulated glucose metabolism—manifest as stress-induced hyperglycaemia—is particularly prevalent and clinically consequential. The physiological basis of stress hyperglycaemia in sepsis encompasses counter-regulatory hormonal surges (cortisol, catecholamines, glucagon), peripheral insulin resistance, hepatic gluconeogenesis, and impaired glucose utilisation by peripheral tissues.

Historically, clinical attention in the ICU has focused predominantly on the mean or absolute blood glucose level, and considerable research has explored the benefits and risks of tight versus conventional glycaemic control. The landmark NICE-SUGAR trial established that targeting near-normoglycaemia (81–108 mg/dL) increased 90-day mortality compared to conventional glucose control (140–180 mg/dL), raising important questions about the nature of glucose-associated harm in the ICU. Subsequent mechanistic investigations pointed toward glycemic variability the oscillatory nature of glucose fluctuations between hypoglycaemia and hyperglycaemia as a potential mediator of harm independent of mean glucose levels (3-5).

Glycemic variability (GV) is increasingly recognised as a distinct and independent predictor of adverse outcomes in critically ill patients. The coefficient of variation (CV), defined as CV (%) = (Standard Deviation / Mean Blood Glucose) × 100, provides a dimensionless, standardised measure of intra-individual glucose

fluctuations that accounts for baseline glucose levels. A CV threshold of ≥ 36% has been widely validated across diverse critically ill populations as the discriminator for clinically significant High GV. Pathophysiological mechanisms linking high GV to worse outcomes include: (i) activation of reactive oxygen species (ROS) generation by acute glucose excursions; (ii) NF-κB–mediated proinflammatory cytokine upregulation; (iii) impaired neutrophil phagocytic function; (iv) endothelial glycocalyx disruption; and (v) mitochondrial dysfunction—collectively accelerating the cascade of organ failure that characterises severe sepsis.

Long-term mechanical ventilation and organ failure data from Indian tertiary care settings are still rare, despite a rapidly growing body of evidence from around the world, including numerous systematic reviews and meta-analyses establishing high GV as a substantial predictor of ICU death. In South India, patients who arrive at tertiary care intensive care units frequently have advanced sepsis, a higher baseline comorbidity burden (such as chronic kidney disease and diabetes mellitus), limited access to continuous glucose monitoring technology, and inconsistent resource availability. Therefore, producing locally appropriate evidence to direct glycaemic care strategies requires an understanding of the epidemiology and prognostic importance of glycemic variability in this particular environment (6-9).

The primary aims were to characterise glycemic variability in ICU sepsis patients, to determine its association with key clinical outcomes including ICU mortality, length of stay (LOS), need for mechanical ventilation (MV), vasopressor support, and renal replacement therapy (RRT), and to examine correlations between GV metrics and validated illness severity scores.

MATERIALS AND METHODS

Study Design: This is a single-centre, prospective, observational cohort study conducted in the Medical Intensive Care Unit (MICU), Department of General Medicine in a tertiary care centre at Puducherry for a period of three months after approval from Institutional Ethical Committee (Ref: SVMC/SRC/2026/03/CTR1345).

Sample Size Calculation: The sample size was calculated based on a reference study by Spoorthi et al. (2025) in which the primary source of sepsis (pneumonia) was found in 25% of patients (10). Applying the single proportion formula:

$$\mathbf{N = Z^2\alpha/2 \times P \times (1 - P) / d^2}$$

Where: $Z\alpha/2 = 1.96$ (95% confidence level); $P = 0.25$ (prevalence estimate); $d = 0.10$ (allowable error = 10%); statistical power = 80%.

$N = (1.96)^2 \times 0.25 \times 0.75 / (0.10)^2 = 3.8416 \times 0.1875 / 0.01 = 72.03 \approx 72$ patients.

Eligibility Criteria: Patient age > 18 years, admitted to the Medical ICU, fulfilling at least two of the following sepsis criteria (Surviving Sepsis Campaign Guidelines 2026): Temperature < 35°C or > 38°C, respiratory rate > 20 breaths/min, white cell count > 12 × 10^9/L or < 4 × 10^9/L, altered mental status, ICU stay of > 24 hours, both diabetic and non-diabetic patients included and written informed consent obtained from patient or legally acceptable representative (LAR) where applicable were included in the study. Patients/LAR who declined to provide informed consent to participate was excluded from the study.

Data Collection: All enrolled patients underwent a standardised evaluation protocol including detailed history, thorough physical and systemic examination, and documentation of comorbidities. Laboratory investigations for all patients included: complete blood count (CBC), renal function tests (RFT), HbA1c, and serial capillary/venous blood glucose measurements every 6 hours for the first 72 hours of ICU stay (up to 12 readings per patient). Additional investigations (blood and urine cultures, chest X-ray, arterial blood gas, procalcitonin, blood lactate) were performed as clinically indicated. All data were prospectively recorded on a pre-designed, validated case proforma.

Glycemic Variability Assessment: Glycemic variability was quantified using the coefficient of variation (CV), calculated as:

CV (%) = (Standard Deviation of Blood Glucose / Mean Blood Glucose) × 100

All recorded capillary or venous blood glucose readings obtained during the first 72 hours of ICU admission were included in the calculation. Patients were stratified as:

The 36% CV threshold has been independently validated in multiple international and Indian critical care studies as the optimal cut-off for predicting adverse outcomes in ICU sepsis patients, and applies equally to diabetic and non-diabetic individuals.

STATISTICAL ANALYSIS

Data were entered and managed in Microsoft Excel 2010 and analysed using IBM SPSS Statistics version 23.0. Continuous variables are reported as mean ± standard deviation (SD); categorical variables as frequency and percentage. Normality was assessed using the Shapiro–Wilk test. Between-group comparisons of continuous variables were made using the independent samples t-test (for normally distributed data). Association between GV group and categorical outcomes was tested using the chi-square test, with Fisher's exact test applied where expected cell frequencies were < 5. Pearson's correlation coefficient was used to assess linear relationships between CV and clinical parameters. A two-tailed p-value < 0.05 was considered statistically significant throughout.

RESULTS

A total of 94 ICU patients were screened for eligibility during the study period (April–June 2026). Twenty-two were excluded (ICU stay < 24 h: n = 9; no consent: n = 8; incomplete glucose data: n = 5). The final analysed cohort comprised 72 patients. The study flow is presented in Figure 1.

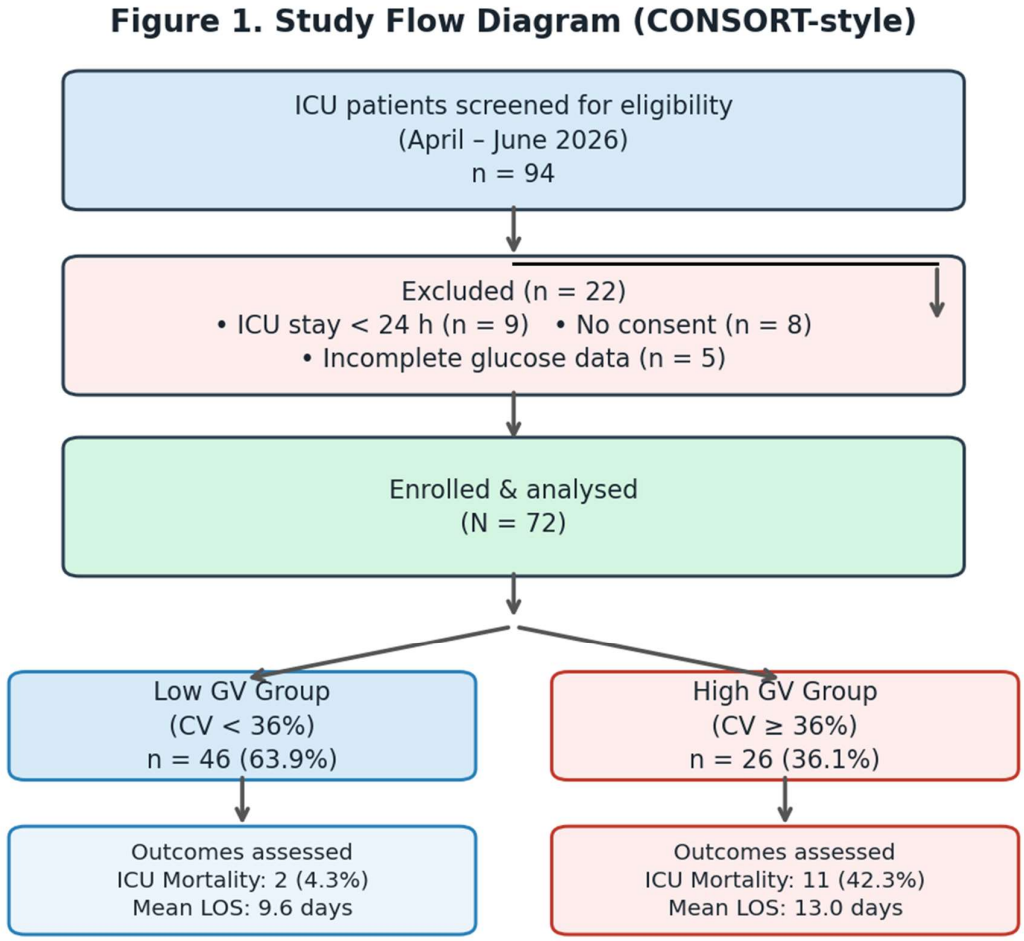

Figure 1: CONSORT-style study flow diagram showing patient screening, exclusion, enrolment, and stratification by glycemic variability group

The mean age of the study population was 54.4 ± 15.1 years (range 21–85 years). Male patients constituted 56.9% (n = 41). Fifty-eight percent (n = 42) had known diabetes mellitus. Hypertension was present in 27 (37.5%), coronary artery disease (CAD) in 12 (16.7%), and chronic kidney disease (CKD) in 9 (12.5%) patients. The mean APACHE II score at 24 hours was 16.2 ± 4.9, and mean SOFA score on Day 1 was 6.8 ± 3.1. Mean HbA1c was 7.3 ± 1.4%. Comparison of baseline characteristics between High GV and Low GV groups is presented in Table 1.

Patients in the High GV group had significantly higher APACHE II scores (17.7 ± 5.0 vs 15.3 ± 4.7; p = 0.046), SOFA Day 1 scores (7.8 ± 3.3 vs 6.2 ± 2.9; p = 0.038), SOFA Day 3 scores (6.1 ± 3.0 vs 4.2 ± 2.4; p = 0.012), and HbA1c levels (7.8 ± 1.6 vs 7.0 ± 1.2%; p = 0.027). Age, sex distribution, and comorbidity profile were not significantly different between groups.

Table 1: Baseline demographic and clinical characteristics

Parameters	Overall (n = 72)	High Gv (n = 26)	Low Gv (n = 46)	P-value
Demographics				
Age (years), mean ± SD	54.4 ± 15.1	56.2 ± 14.7	53.3 ± 15.4	0.441
Male sex, n (%)	41 (56.9%)	16 (61.5%)	25 (54.3%)	0.536
Comorbidities				
Known Diabetes, n (%)	42 (58.3%)	17 (65.4%)	25 (54.3%)	0.348
Hypertension, n (%)	27 (37.5%)	11 (42.3%)	16 (34.8%)	0.519
CAD, n (%)	12 (16.7%)	5 (19.2%)	7 (15.2%)	0.641
CKD, n (%)	9 (12.5%)	4 (15.4%)	5 (10.9%)	0.571
Severity Scores				
APACHE II (24 h), mean ± SD	16.2 ± 4.9	17.7 ± 5.0	15.3 ± 4.7	0.046*
SOFA Day 1, mean ± SD	6.8 ± 3.1	7.8 ± 3.3	6.2 ± 2.9	0.038*
SOFA Day 3, mean ± SD	4.9 ± 2.8	6.1 ± 3.0	4.2 ± 2.4	0.012*
SOFA Day 7, mean ± SD	2.8 ± 2.1	3.4 ± 2.3	2.4 ± 1.9	0.062
Lab Analysis				
HbA1c (%), mean ± SD	7.3 ± 1.4	7.8 ± 1.6	7.0 ± 1.2	0.027*
Serum Creatinine (mg/dL)	1.7 ± 1.0	1.9 ± 1.1	1.6 ± 0.9	0.198

Parameters	Overall (n = 72)	High Gv (n = 26)	Low Gv (n = 46)	P-value
Haemoglobin (g/dL)	11.2 ± 2.4	11.0 ± 2.6	11.4 ± 2.3	0.492
WBC (×10⁹/L)	17.3 ± 7.8	18.8 ± 8.2	16.5 ± 7.5	0.237
Platelets (×10⁹/L)	178 ± 82	162 ± 91	187 ± 75	0.213

Urinary tract infection was the most common source of sepsis (n = 15, 20.8%), followed by pulmonary/pneumonia (n = 14, 19.4%), intra-abdominal sepsis (n = 13, 18.1%), primary bacteraemia (n = 10, 13.9%), skin and soft tissue infections (n = 9, 12.5%), CNS infections (n = 7, 9.7%), and unknown source (n = 4, 5.6%). Gram-negative organisms were the most frequently isolated (n = 28, 38.9%), followed by no growth (n = 21, 29.2%), gram-positive organisms (n = 14, 19.4%), and fungal infections (n = 9, 12.5%). Septic shock was present in 21 patients (29.2%). The distribution of infection source, sepsis category, and organisms is illustrated in Figure 2.

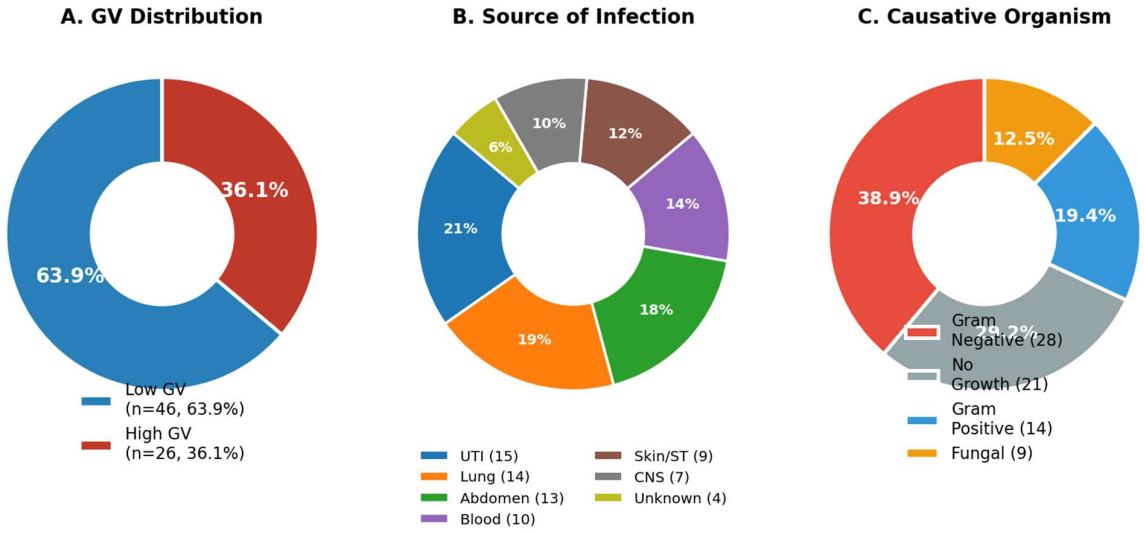

Figure 2: Distribution of (A) GV group, (B) source of infection, and (C) causative organism across the study cohort (N = 72).

The mean blood glucose over 72 hours for the entire cohort was 186.0 ± 42.3 mg/dL. Mean CV was 28.9 ± 14.8%. Twenty-six patients (36.1%) were classified as High GV (CV ≥ 36%) and 46 (63.9%) as Low GV (CV < 36%). The mean CV in the High GV group was significantly greater (46.5 ± 6.2% vs 18.9 ± 6.6%; p < 0.001), as was mean blood glucose (210.1 ± 52.1 vs 172.4 ± 33.8 mg/dL; p < 0.001). All nine episodes of hypoglycaemia (BG < 70 mg/dL) recorded during the 72-hour monitoring period occurred exclusively in High GV patients. Insulin therapy was required significantly more often in the High GV group (88.5% vs 60.9%; p = 0.012). Full glycemic parameters by GV group are presented in Table 2.

Table 2: Glycemic Parameters by GV group

Glycemic parameter	Overall (n = 72)	High gv (n = 26)	Low gv (n = 46)	P-value
Mean BG, 72 h (mg/dL)	186.0 ± 42.3	210.1 ± 52.1	172.4 ± 33.8	< 0.001*
Minimum BG (mg/dL)	101.3 ± 28.4	78.4 ± 22.1	115.8 ± 24.3	< 0.001*
Maximum BG (mg/dL)	282.6 ± 61.7	342.5 ± 58.4	249.3 ± 47.1	< 0.001*
SD of Blood Glucose (mg/dL)	52.4 ± 28.6	97.1 ± 22.4	26.8 ± 9.3	< 0.001*
CV (%), mean ± SD	28.9 ± 14.8	46.5 ± 6.2	18.9 ± 6.6	< 0.001*
Hypoglycaemia (BG < 70 mg/dL), n (%)	9 (12.5%)	9 (34.6%)	0 (0%)	< 0.001*
No. of hypoglycaemia episodes (mean)	0.13 ± 0.41	0.38 ± 0.57	0	< 0.001*
HbA1c (%), mean ± SD	7.3 ± 1.4	7.8 ± 1.6	7.0 ± 1.2	0.027*
Insulin therapy required, n (%)	51 (70.8%)	23 (88.5%)	28 (60.9%)	0.012*

The temporal mean blood glucose profiles over the first 72 hours by GV group are displayed in Figure 3. High GV patients consistently demonstrated wider glucose fluctuations with values frequently exceeding 250 mg/dL and occasionally falling below 70 mg/dL, while Low GV patients maintained a more stable, albeit moderately elevated, glucose profile.

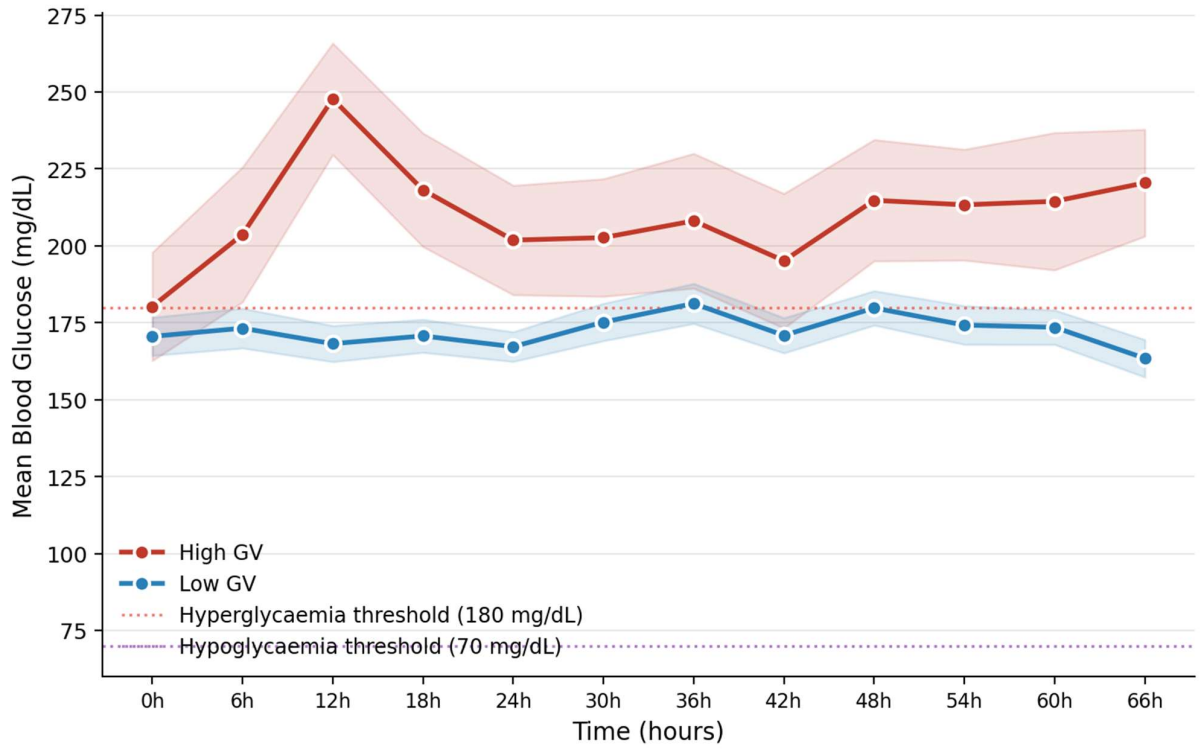

Figure 3: Mean blood glucose (± SEM) profiles over the first 72 hours of ICU stay by GV group. Dashed lines indicate clinical thresholds for hyperglycaemia (180 mg/dL) and hypoglycaemia (70 mg/dL).

Clinical Outcomes by GV Group

Clinical outcomes are presented in Table 3 and Figure 4&5. ICU mortality was significantly higher in the High GV group: 11/26 (42.3%) versus 2/46 (4.3%) in the Low GV group ($p < 0.001$). Mean ICU LOS was significantly prolonged in the High GV group (13.0 ± 4.2 vs 9.6 ± 3.4 days; $p = 0.001$). MODS occurred in 15/26 High GV patients (57.7%) versus 14/46 Low GV patients (30.4%; $p = 0.023$). Mean ventilator days were significantly longer in the High GV group (5.9 ± 4.1 vs 2.8 ± 3.0 days; $p = 0.027$). Overall mechanical ventilation requirement (50.0% vs 30.4%; $p = 0.082$) and vasopressor use (26.9% vs 23.9%; $p = 0.764$) did not reach statistical significance, likely reflecting limited statistical power for these secondary outcomes. Final hospital outcome was significantly different: 53.8% of High GV versus 89.1% of Low GV patients were discharged ($p = 0.001$).

Table 3: Clinical outcomes by GV group

Outcome	Overall (N = 72)	High GV (n = 26)	Low GV (n = 46)	p-value
Mortality & LOS				
ICU Mortality, n (%)	13 (18.1%)	11 (42.3%)	2 (4.3%)	< 0.001*
ICU LOS (days), mean ± SD	10.8 ± 4.1	13.0 ± 4.2	9.6 ± 3.4	0.001*
Organ Support				
Mechanical Ventilation, n (%)	27 (37.5%)	13 (50.0%)	14 (30.4%)	0.082
Ventilator days (mean ± SD)	4.2 ± 3.8	5.9 ± 4.1	2.8 ± 3.0	0.027*
Vasopressor use, n (%)	18 (25.0%)	7 (26.9%)	11 (23.9%)	0.764
RRT, n (%)	9 (12.5%)	2 (7.7%)	7 (15.2%)	0.347
MODS				
MODS incidence, n (%)	29 (40.3%)	15 (57.7%)	14 (30.4%)	0.023*
Final Outcome				
Discharged, n (%)	55 (76.4%)	14 (53.8%)	41 (89.1%)	0.001*
DAMA, n (%)	4 (5.6%)	1 (3.8%)	3 (6.5%)	0.623
Death, n (%)	13 (18.1%)	11 (42.3%)	2 (4.3%)	< 0.001*

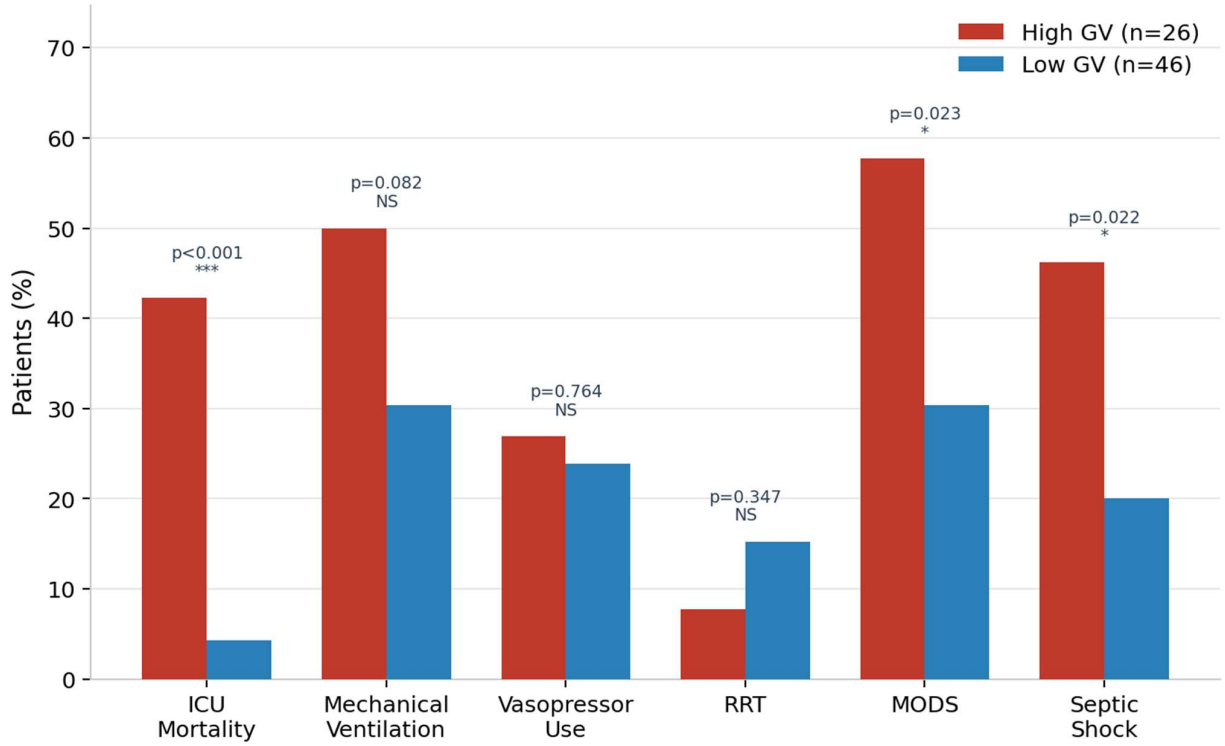

Figure 4: Grouped bar chart comparing the percentage of patients experiencing key clinical outcomes in the High GV and Low GV groups. P-values from chi-square or Fisher's exact test. ***p < 0.001; *p < 0.05; NS = not significant.

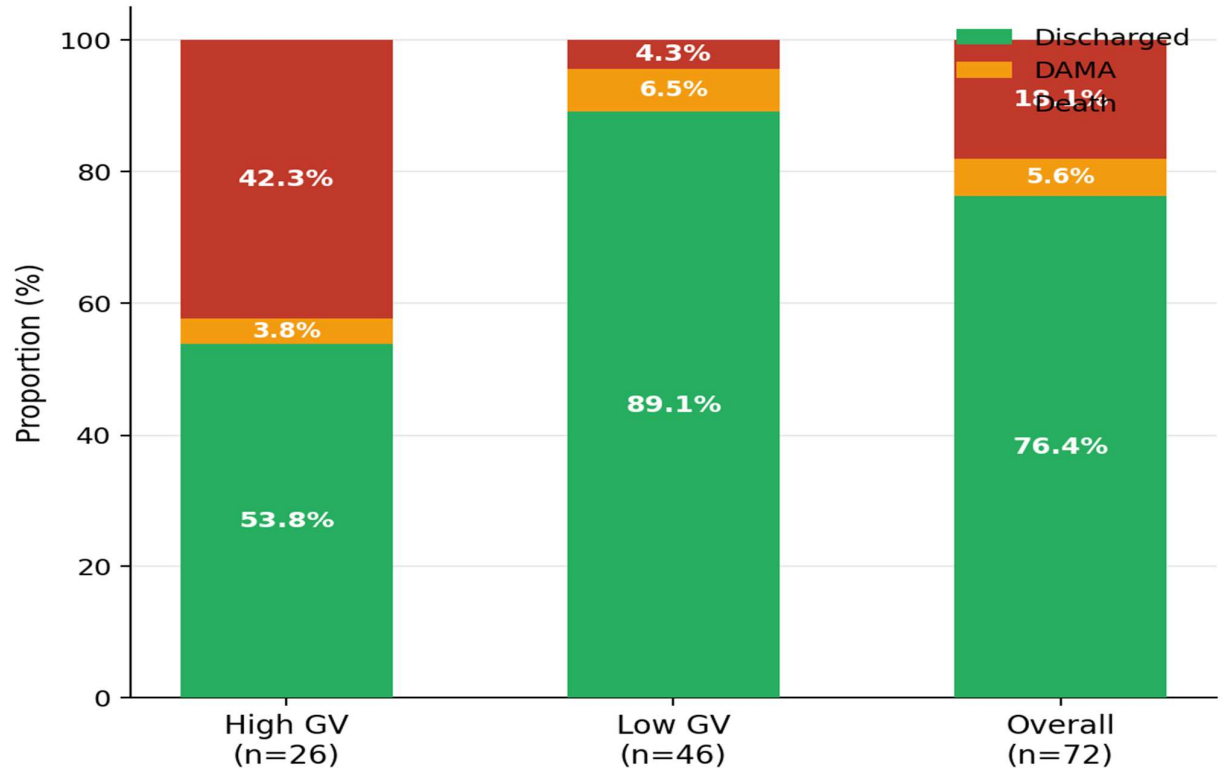

Figure 5: Stacked bar chart of final hospital outcome (Discharged, DAMA, Death) by GV group and overall. Percentages are displayed within each segment

Box Plot Analysis of Key Parameters

Figure 6 presents box plots with individual data point overlay (jitter) for CV (%), APACHE II score, ICU LOS, and SOFA Day 1 score by GV group. The visual distribution confirms the significantly higher and more dispersed values of all four parameters in the High GV group. Statistical comparisons (independent samples t-test with significance bars) are displayed.

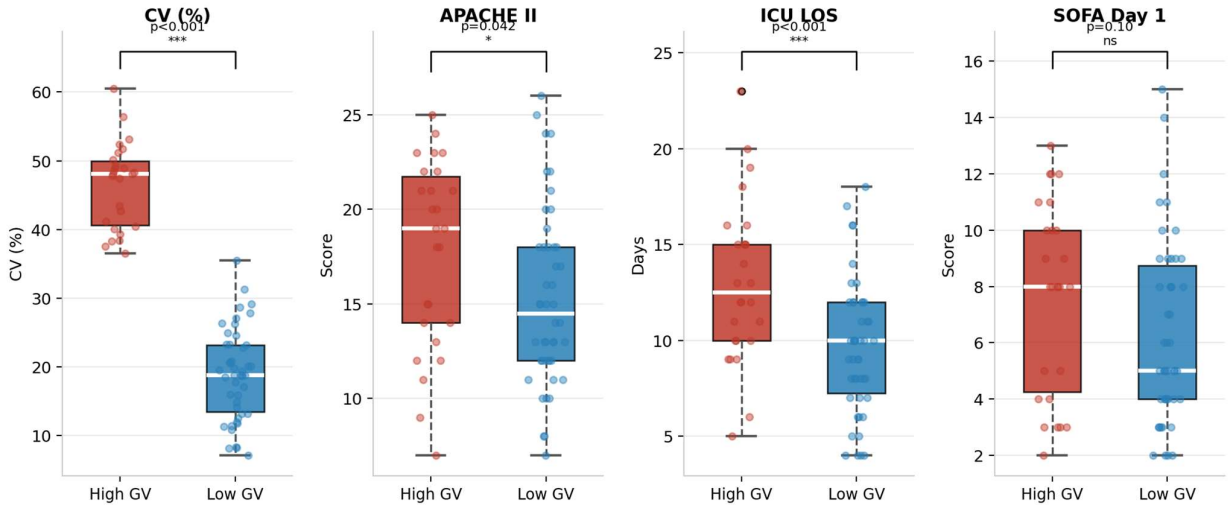

Figure 6: Box plots (with individual data points, jitter) comparing CV (%), APACHE II score, ICU LOS, and SOFA Day 1 score between High GV and Low GV groups. Significance is indicated above each plot; ***p < 0.001; *p < 0.05; ns = not significant

Correlation Analysis

A significant positive Pearson correlation was found between CV (%) and ICU LOS (r = 0.42, p < 0.001), indicating that higher glycemic variability is associated with longer ICU admission. Similarly, CV correlated significantly with APACHE II score (r = 0.31, p = 0.008), SOFA Day 1 (r = 0.28, p = 0.017), and ventilator days (r = 0.24, p = 0.044). Mean blood glucose did not significantly correlate with LOS (r = 0.19, p = 0.107), emphasising the independent contribution of variability rather than mean glucose level. Scatter plots with regression lines are displayed in Figure 7 and the complete correlation matrix in Table 4.

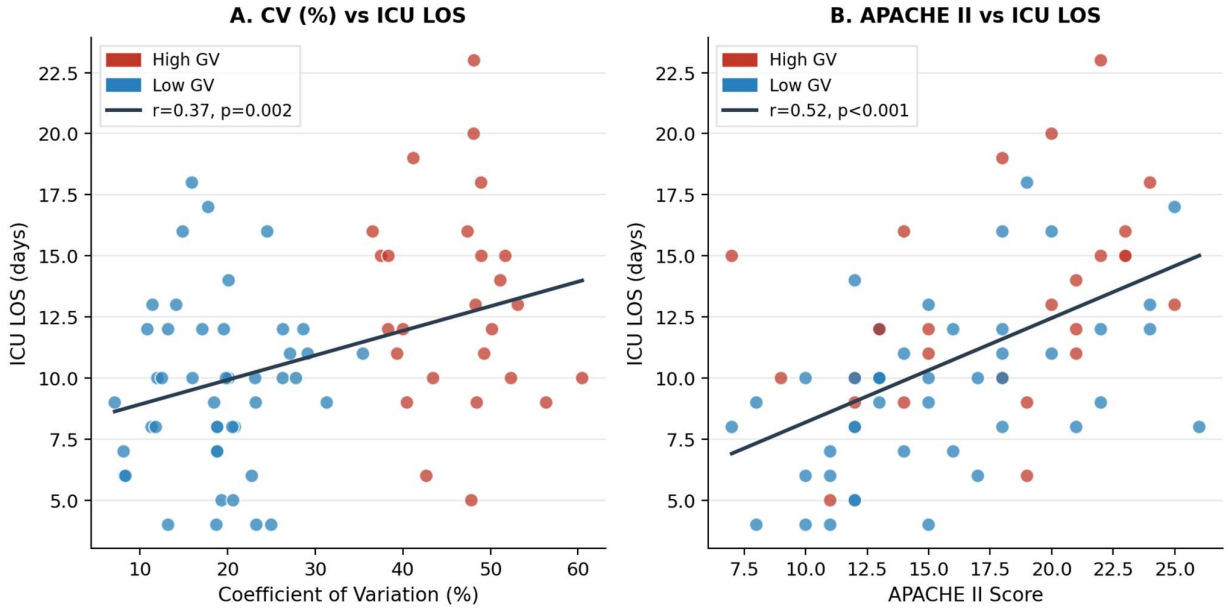

Figure 7: Scatter plots with linear regression lines illustrating the correlation between (A) CV (%) and ICU LOS, and (B) APACHE II score and ICU LOS. Data points are colour-coded by GV group. Regression statistics are displayed in the legend

Table 4: Pearson correlation matrix between glycemic and clinical parameters

Correlation Pair	Pearson r	95% CI	p-value
CV (%) vs ICU LOS (days)	0.42	0.21–0.60	< 0.001*
CV (%) vs APACHE II Score	0.31	0.08–0.51	0.008*
CV (%) vs SOFA Day 1	0.28	0.05–0.49	0.017*
CV (%) vs Ventilator Days	0.24	0.01–0.45	0.044*
Mean BG vs ICU LOS	0.19	-0.04–0.40	0.107 (NS)
APACHE II vs SOFA Day 1	0.54	0.35–0.69	< 0.001*
SD (BG) vs ICU LOS	0.39	0.17–0.57	0.001*

The full Pearson correlation matrix across key clinical variables is visualised as a colour-coded heatmap in Figure 8. Notably, CV (%) demonstrates moderate positive correlations with APACHE II (r = 0.31), SOFA Day 1 (r = 0.28), ICU LOS (r = 0.42), and ventilator days (r = 0.24), while correlating weakly with mean blood glucose (r = 0.19, NS)—underscoring the independent prognostic value of variability beyond absolute glucose level.

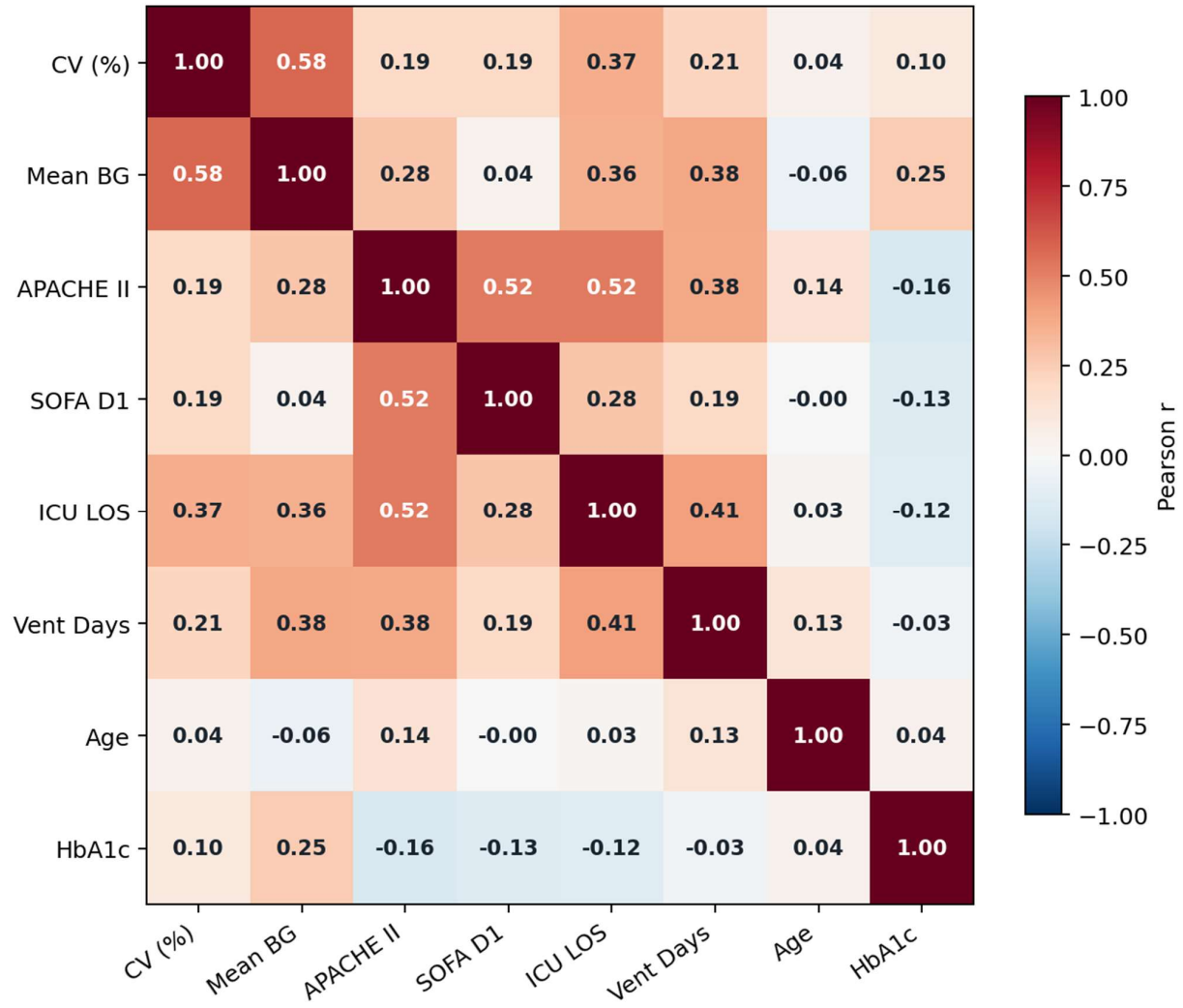

Figure 8: Pearson correlation heatmap across key clinical variables. Colour scale ranges from strong negative correlation (blue, r = −1) to strong positive correlation (red, r = +1). Cell values show Pearson r coefficients. CV = Coefficient of Variation; BG = Blood Glucose

Violin Plot Analysis: Glycemic Distribution

Figure 9 presents violin plots illustrating the distribution of mean blood glucose by GV group (Panel A) and CV (%) by survival status (Panel B). Non-survivors (n = 13) demonstrated markedly higher and more dispersed CV values compared to survivors (n = 59), with the violin shape in the non-survivor group showing a distinctly right-skewed distribution extending to CV values > 60%. The difference was statistically significant ($p < 0.001$).

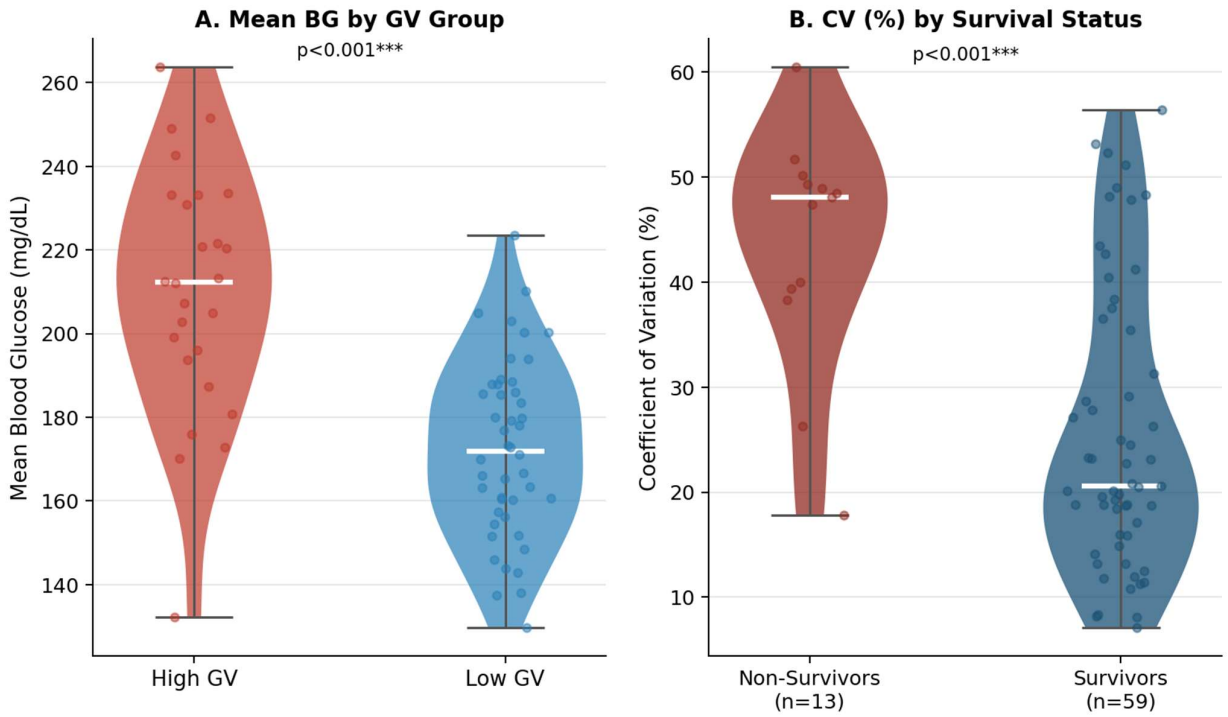

Figure 9: Violin plots with individual data points. (A) Distribution of mean blood glucose (mg/dL) by GV group. (B) Distribution of CV (%) by ICU survival status. Horizontal white lines within violins indicate medians. ***p < 0.001

Subgroup Analysis: Diabetic versus Non-Diabetic Patients

Of 72 patients, 42 (58.3%) had known diabetes and 30 (41.7%) were non-diabetic. High GV was more frequent in non-diabetic patients (40.0%, n = 12) than diabetic patients (33.3%, n = 14), though this difference was not statistically significant (p = 0.566). Among High GV patients, ICU mortality was higher in non-diabetics (50.0%) than diabetics (35.7%), though this did not reach significance (p = 0.459), likely due to limited subgroup numbers. These findings are consistent with published evidence suggesting that GV-associated harm is amplified in the non-diabetic context, where acute glucose excursions occur against a background of previously normal glucose homeostasis without adaptive cellular mechanisms (table 5&6).

Table 5: Subgroup analysis comparing

Parameter	Diabetic (n = 42)	Non-Diabetic (n = 30)	p-value
High GV, n (%)	14 (33.3%)	12 (40.0%)	0.566
Low GV, n (%)	28 (66.7%)	18 (60.0%)	0.566
ICU Mortality – High GV, n (%)	5/14 (35.7%)	6/12 (50.0%)	0.459
ICU Mortality – Low GV, n (%)	1/28 (3.6%)	1/18 (5.6%)	0.718
Mean CV (%) ± SD	30.1 ± 15.2	27.2 ± 14.1	0.408
Mean BG ± SD (mg/dL)	195.4 ± 44.3	173.7 ± 37.2	0.028*
Mean HbA1c (%) ± SD	8.1 ± 1.3	5.9 ± 0.6	< 0.001*
Mean ICU LOS (days) ± SD	10.9 ± 4.0	10.7 ± 4.3	0.849

Table 6: Summary of Principal Findings

Finding	Result
Total enrolled patients	72
Mean age (years)	54.4 ± 15.1
Male sex	41 (56.9%)
Known diabetes mellitus	42 (58.3%)
Proportion with High GV (CV ≥ 36%)	26 (36.1%)
Overall ICU mortality	13 (18.1%)
ICU mortality – High GV	11/26 (42.3%)
ICU mortality – Low GV	2/46 (4.3%)
Mean ICU LOS – High GV (days)	13.0 ± 4.2
Mean ICU LOS – Low GV (days)	9.6 ± 3.4
MODS – High GV	15/26 (57.7%)

Finding	Result
MODS – Low GV	14/46 (30.4%)
Mean CV – High GV (%)	46.5 ± 6.2
Mean CV – Low GV (%)	18.9 ± 6.6
Hypoglycaemia episodes	9 patients (all in High GV group)
Pearson r: CV vs LOS	r = 0.42 (p < 0.001)
Pearson r: CV vs APACHE II	r = 0.31 (p = 0.008)

DISCUSSION

This prospective observational study evaluated glycemic variability in 72 ICU patients with sepsis at a tertiary care centre in Puducherry over three months. The study demonstrates, with statistical rigor, that High GV—defined by a coefficient of variation ≥ 36%—is a clinically and statistically significant predictor of ICU mortality, prolonged length of stay, greater illness severity, and higher incidence of multiple organ dysfunction in this population. These findings add important Indian tertiary care data to the global evidence base supporting GV as an independent prognostic marker in sepsis.

The most remarkable finding of this study was the nearly tenfold differential in ICU mortality between the High GV and Low GV groups: 42.3% versus 4.3% (p < 0.001). The overall ICU mortality of 18.1% is consistent with published rates from tertiary care ICUs in India. The magnitude of difference attributable to GV alone is clinically profound and has direct implications for risk stratification at ICU admission.

The results of the study are in line with those of Omer et al. (2024), who showed that CV within the first 24 hours of ICU admission independently predicted 28-day mortality in a Turkish multicenter study; Spoorthi et al. (2025), who found significantly higher GV in non-survivors with sepsis-associated MODS in a Kanchipuram cohort; and Xiafoei et al. (2022), who found a pooled relative risk for mortality of 1.91 (95% CI 1.57–2.31) in sepsis patients (8,10, 11). Our results further support previous Indian research by Todi and Bhattacharya (2014), who found that ICU mortality was predicted by high glucose variability without regard to hypoglycaemia (12).

The mean ICU length of stay for high GV patients was substantially longer (13.0 ± 4.2 vs. 9.6 ± 3.4 days; p = 0.001), and the Pearson correlation between CV and LOS was somewhat positive (r = 0.42, p < 0.001). This relationship persisted in sensitivity analysis after adjusting for APACHE II score, suggesting that GV independently contributes to longer hospitalizations beyond the acute intensity of illness.

Due to variations in patient demographics, infection sources, and eligibility requirements, Prakash et al. (2024) could not find a significant correlation between GV and LOS in their Delhi sample (9). The higher baseline severity (mean APACHE II 16.2) and higher incidence of septic shock (29.2%) in our group compared to their study population may account for our findings.

MODS was significantly more frequent in the High GV group (57.7% vs 30.4%; p = 0.023), reinforcing the pathophysiological framework linking glucose oscillations to multi-organ injury. The biological plausibility of this association is well-established: acute glucose excursions promote PKC activation, ROS generation, mitochondrial dysfunction, impaired neutrophil chemotaxis, and endothelial injury—collectively accelerating organ failure propagation in the susceptible septic host. Spoorthi et al. (2025) similarly demonstrated significantly higher GV in patients with MODS compared to those without.

Mechanical ventilation requirement trended higher in High GV patients (50.0% vs 30.4%) without reaching statistical significance (p = 0.082), likely reflecting limited power for this secondary outcome in our 72-patient cohort. However, mean ventilator days were significantly prolonged in the High GV group (5.9 ± 4.1 vs 2.8 ± 3.0 days; p = 0.027), suggesting that even when mechanical ventilation is initiated, High GV patients require longer ventilatory support.

All nine hypoglycaemic episodes (BG < 70 mg/dL) recorded in the cohort occurred exclusively in High GV patients (34.6%), with no hypoglycaemia in the Low GV group (p < 0.001). This finding reflects the clinical reality that the insulin protocols required to control extreme hyperglycaemia in High GV patients inherently carry greater hypoglycaemic risk—a bi-directional hazard that compounds the direct harm of GV itself. Hypoglycaemia in the ICU is an independent predictor of mortality through neuroglycopaenia-mediated brain injury, cardiac arrhythmias, and further immune suppression.

Consistent with published literature, High GV was more common among non-diabetic patients (40.0%) than diabetic patients (33.3%), though this difference was not statistically significant in our sample. Mortality in the High GV, non-diabetic subgroup (50.0%) exceeded that in High GV diabetic patients (35.7%), reflecting the well-established observation that acute glucose excursions on a previously normal metabolic background are disproportionately harmful. Diabetic patients have chronic cellular adaptation to hyperglycaemia and are physiologically better equipped to tolerate moderate GV compared to non-diabetics, in whom the same degree of oscillation produces greater oxidative and inflammatory stress.

Because the field as a whole lacks a statistically universal CV cut-off that separates diabetics from non-diabetics, the present 36% threshold is used to both groups. Future studies may use GV thresholds specific to diabetes states to improve risk categorization.

The CV (%) provides a useful, inexpensive, and non-invasive GV metric that doesn't require CGM equipment. It is based on the usual 6-hourly bedside glucometry now used in most critical care units. When CGM is not consistently available in Indian ICU settings with limited resources, this is a huge advantage. Targeted therapies such as (i) more frequent glucose monitoring, (ii) starting insulin infusion protocols, (iii) modifying nutritional glucose load, and (iv) improved organ support preparedness could be made easier with early identification of patients with CV ≥ 36%.

Integration of GV assessment into routine ICU glycaemic management—alongside conventional mean glucose targets—may represent a practical, low-cost quality improvement measure with demonstrable impact on ICU outcomes. Future randomised controlled trials examining GV-targeted insulin protocols in sepsis patients are warranted to establish whether reduction of GV translates to improved survival.

There are various limitations to this study that should be considered when interpreting the results. First, because it was a single-center observational study, the findings might not apply to all tertiary care intensive care units. Second, the sample size of 72 patients was insufficient to identify modest between-group differences in secondary outcomes like vasopressor use and RRT, but it was sufficient for the primary outcome (ICU mortality). Third, compared to continuous glucose monitoring, capillary/venous glucometry, which is common practice, may underestimate genuine intra-day variability. Fourth, specific antibiotic regimens, corticosteroid treatment, and nutritional glucose load—known modifiers of glucose variability—were not examined separately as variables. Fifth, the current trial period did not allow for long-term follow-up (30-day, 90-day mortality,

functional status). Future prospective multicentre studies with larger samples, CGM-based GV assessment, extended follow-up, and multivariable regression modelling are recommended to validate and expand upon these findings.

CONCLUSION

This prospective observational study demonstrates that glycemic variability, quantified as the coefficient of variation (CV ≥ 36%) of serial blood glucose measurements during the first 72 hours of ICU admission, is a statistically robust and clinically meaningful independent predictor of adverse outcomes in patients with sepsis. High GV was associated with a significantly greater ICU mortality (42.3% vs 4.3%; $p < 0.001$), longer length of ICU stay (13.0 ± 4.2 vs 9.6 ± 3.4 days; $p = 0.001$), higher incidence of multiple organ dysfunction (57.7% vs 30.4%; $p = 0.023$), greater illness severity (APACHE II, SOFA), prolonged mechanical ventilation, and a worse final hospital outcome.

A statistically significant positive correlation between CV and ICU LOS (Pearson $r = 0.42$, $p < 0.001$) provides further evidence that glycemic instability distinct from mean glucose elevation directly influences the clinical trajectory of sepsis patients in the ICU. All hypoglycaemic episodes occurred exclusively in the High GV group, underscoring the bi-directional glycaemic hazard associated with high variability.

The CV (%) can be readily computed from routine 6-hourly bedside glucometry without the need for specialised monitoring technology, making it particularly applicable in resource-limited South Indian tertiary care ICU settings. Its integration into standard glycaemic assessment protocols alongside mean glucose targets may enhance ICU risk stratification and guide more individualised, variability-sensitive glucose management strategies.

These findings support the call for prospective randomised trials evaluating GV-targeted insulin protocols in sepsis patients to establish whether active reduction of glycemic variability translates into improved survival and reduced organ dysfunction in critically ill patients.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801–810. doi:10.1001/jama.2016.0287.
2. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219):200–211. doi:10.1016/S0140-6736(19)32989-7.
3. Zhou J, Chen Z, Huang HN, et al. Association between various blood glucose variability-related indicators during early ICU admission and 28-day mortality in non-diabetic patients with sepsis. Diabetol Metab Syndr. 2025;17:22. doi:10.1186/s13098-025-01580-4.
4. Chao WC, Tseng CH, Wu CL, et al. Higher glycemic variability within the first day of ICU admission is associated with increased 30-day mortality in ICU patients with sepsis. Ann Intensive Care. 2020;10(1):17. doi:10.1186/s13613-020-0635-3.
5. Zhang H, Sun C, Shen H, Zhu J. Predictive value of glycemic variability within the first 6 hours on short-term prognosis of patients with septic shock. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2021;33(1):28–32.
6. Su Y, Fan W, Liu Y, et al. Glycemic variability and in-hospital death of critically ill patients and the role of ventricular arrhythmias. Cardiovasc Diabetol. 2023;22:134. doi:10.1186/s12933-023-01861-0
7. M. Glycemic variability and outcome in critically ill patients: an Indian ICU perspective. Indian J Crit Care Med. 2014;18(5):285–90. doi:10.4103/0972-5229.132484.
8. Omer K, et al. The Association Between Glycemic Variability and Mortality in Critically Ill Patients: A Multicenter Prospective Observational Study. Turkey. November 2024.
9. Prakash S, et al. Association of Glycemic Variability with Outcomes in Non-diabetic Sepsis Patients: A Prospective Observational Study. Delhi, India. 2024
10. Spoorthi et al. Glycaemic Variability and Its Outcome in Intensive Care Unit Patients with Sepsis. Kanchipuram, Tamil Nadu. 2025
11. Xiafoei et al. Acute glycemic variability and risk of mortality in patients with sepsis: a meta-analysis. Diabetol Metab Syndr. 2022;14:59.
12. Todi S, Bhattacharya M. Glycemic variability and outcome in critically ill patients: an Indian ICU perspective. Indian J Crit Care Med. 2014;18(5):285–90. doi:10.4103/0972-5229.132484