

Glycemic Gap as a Predictor of Outcome in Critically Ill Patients with Type 2 Diabetes Mellitus

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Abstract:

Objective: To evaluate the association between glycemic gap and clinical outcomes in critically ill patients with type 2 diabetes mellitus.

Material and Methods: This prospective study was conducted at a tertiary care centre in South India. A total of 100 critically ill patients with diabetes mellitus admitted to the intensive care unit (ICU) between February 2021 and October 2022 were included. Admission blood glucose, HbA1c, A1c-derived average glucose (ADAG), glycemic gap, and acute physiology and chronic health evaluation-II (APACHE II) score were recorded. Patients were followed up until hospital discharge or death, and outcomes were analysed.

Results: Of the 100 patients, 76 survived and 24 were non-survivors (in-hospital). The mean glycemic gap was significantly higher among non-survivors than survivors (97.3 vs. 67.8 mg/dL; p-value=0.018). Patients with a glycemic gap >56 mg/dL had significantly higher mortality and adverse outcomes compared with those with a lower glycemic gap. The glycemic gap showed better discriminatory ability than HbA1c and admission blood glucose, with area under the characteristic curve (AUCs) of 0.672, 0.556, and 0.539, respectively.

Conclusion: A higher glycemic gap was associated with increased mortality and adverse outcomes in critically ill patients with diabetes mellitus. Although its predictive performance was modest, the glycemic gap may serve as a supplementary indicator when used alongside established prognostic scoring systems.

Keywords: APACHE II score, critically ill patients, diabetes mellitus, glycemic gap

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Introduction

Stress-induced hyperglycaemia is frequently observed across a variety of clinical scenarios and represents an adaptive response mediated through immune, neural, and endocrine pathways. This response is intended to ensure adequate metabolic substrate availability for vital organs during periods of physiological stress and critical illness¹. This process is largely driven by a surge of counter-regulatory hormones and pro-inflammatory cytokines, which together increase hepatic glucose production while simultaneously promoting insulin resistance. Under these conditions, glycogenolysis and gluconeogenesis are markedly stimulated; glycogen breakdown is predominantly triggered by elevated catecholamine levels, whereas enhanced gluconeogenesis is mainly attributable to increased glucagon secretion.

In critically ill patients, the associated insulin resistance further exacerbates hyperglycaemia by limiting glucose uptake in skeletal muscle and adipose tissue, largely due to impaired insulin signalling and reduced expression of glucose transporter-4 (GLUT-4) transporters.

Multiple factors contribute to this dysregulated glucose metabolism, including increased secretion of glucagon, growth hormone, catecholamines, and cortisol, along with inflammatory cytokines such as interleukin (IL)-1, IL-6, and tumour necrosis factor- α (TNF- α). Additional influences include nutritional interventions and relative insulin deficiency². Collectively, these changes culminate in hyperglycaemia commonly observed in trauma and critical illness^{1,3}. Acute elevations in blood glucose are associated with adverse clinical outcomes, underscoring the importance of early recognition and appropriate management. Identifying stress-related hyperglycaemia and stratifying high-risk individuals at an early stage may help improve hospital outcomes.

The glycemic gap is a measure used to assess stress-related hyperglycaemia and is calculated as:

Glycemic gap=Admission serum glucose – A1c-derived average glucose (ADAG).

The A1c-derived average glucose (ADAG) is calculated from HbA1c using the standard equation: $ADAG=(28.7 \times HbA1c)-46.7^{4,5}$.

This study evaluated the role of the glycemic gap in determining outcomes among critically ill patients with type 2 diabetes mellitus.

Material and Methods

This prospective study was conducted at a tertiary care hospital in South India after obtaining clearance from the Institutional Ethics Committee (vide letter no. MSRMC/EC/PG-37/01-21). Informed consent was obtained from all study participants.

A total of 100 critically ill patients with diabetes mellitus, aged more than 18 years, admitted to the intensive care unit (ICU) between February 2021 and October 2022 were recruited. Patients with diabetic ketoacidosis (DKA) or hyperosmolar hyper glycaemic state (HHS) at the time of admission, and those receiving systemic corticosteroids, were excluded.

A detailed clinical history was obtained, and a thorough clinical examination was performed for all patients. Plasma glucose levels and HbA1c were measured and recorded at the time of admission. Blood samples for biochemical analysis were collected at admission, according to standard institutional protocols. Random blood glucose was measured using an automated hexokinase-based chemistry analyser (e.g., Beckman Coulter AU5800, USA), and HbA1c was estimated using a high-performance liquid chromatography (HPLC)-based analyser (e.g., Bio-Rad D-10, USA) in the hospital's NABL-accredited clinical biochemistry laboratory. All assays were performed under routine internal and external quality control programmes to ensure accuracy and reproducibility.

The glycemic gap was calculated as the difference between admission blood glucose and the estimated average glucose derived from the HbA1c value, using the formula: $ADAG = (28.7 \times HbA1c) - 46.7$.

The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated for all patients at admission. Patients were followed up throughout their hospital stay. Outcomes including multiorgan dysfunction, need for mechanical ventilation, duration of ICU stay, requirement for inotropic support, and mortality were recorded. Multiorgan failure was defined as the failure of two or more organ systems following an acute threat to systemic homeostasis, requiring medical support for life-sustaining functions. In this study, in-hospital mortality was considered the primary outcome.

Sample size calculation

A study conducted by Wein-Li Lia et al.⁶ reported mortality rates of 9.5% in patients with a lower glycemic gap and 29.5% in those with a higher glycemic gap. Assuming similar proportions, with a power of 90%, a 5% level of significance, and a 10% non-response rate, a minimum sample size of 94 patients was estimated. Accordingly, 100 patients were recruited for the present study.

Statistical analysis

Data were entered into Microsoft Excel and analysed using SPSS software version 22. Categorical variables were expressed as frequencies and percentages, and statistical significance was assessed using the Chi-square test or Fisher's exact test, as appropriate. Continuous variables were expressed as mean $\pm$ standard deviation, and comparisons between two groups were performed using the independent samples t-test.

Receiver operating characteristic (ROC) curves were constructed for the glycemic gap in relation to mortality and were compared with APACHE II score, HbA1c, and random

blood glucose (RBS). From the ROC analysis, optimal cut-off values were identified to estimate sensitivity, specificity, and predictive values. An area under the curve (AUC) of 0.5 indicates discrimination no better than chance, while values above 0.8 suggest good discriminatory ability.

The optimal cut-off point for the glycemic gap in predicting ICU mortality was determined using a data-driven approach. ROC analysis was performed, and the threshold that maximised the Youden index (sensitivity+specificity-1) was selected. This approach enabled the identification of the cut-off value that best discriminated survivors from non-survivors in the study cohort. For robustness, cut-off values reported in prior literature were also examined, and the Youden-derived threshold was found to be consistent with the clinically relevant ranges reported in similar critically ill populations.

To address potential confounding in the association between glycemic gap and in-hospital mortality, multivariate logistic regression analysis was performed. Covariates included age, sex, APACHE II score, admission diagnosis, baseline HbA1c, pre-ICU antihyperglycemic therapy, chronic kidney disease, steroid use, sepsis or infection status, and mechanical ventilation at admission. Covariates were selected a priori based on clinical relevance, prior literature, and directed acyclic graph (DAG) analyses.

Multicollinearity was assessed using variance inflation factors (VIF), and no significant collinearity was observed (all VIF values <5). Model diagnostics included assessment of goodness-of-fit using the Hosmer-Lemeshow test. Missing data (<5%) were handled using complete-case analysis. Sensitivity analyses excluding patients with extreme glycemic gap values and those receiving pre-ICU insulin therapy were performed to assess robustness. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) and p values were reported. Statistical analyses were performed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 100 diabetic patients admitted to the ICU were included in the study. Demographic details, clinical and laboratory parameters, including admission blood glucose and HbA1c, were recorded. APACHE II score on the day of admission and glycemic gap were calculated by subtracting admission glucose from ADAG. $[ADAG = [(28.7 \times HbA1c) - 46.7]]$. Patients were followed up till discharge or death, and adverse outcomes were recorded.

Patients were divided into two groups, survivors and non-survivors (in-hospital), based on the outcomes. Out of 100 patients, 76 were survivors, and 24 were non-survivors. Baseline characteristics like age, gender, comorbidities, and glycemic gap were compared between the two groups (Table 1). The majority of patients belonged to the age group 51–70 years. Mean age among survivors and non-survivors was 64.2 ± 12.3 and 60.9 ± 13.2 , respectively (p -value=0.260). Among 100 ICU patients in this study, 57 were male patients, and 43 were female patients; 43 males (75.4%) were in the survivor group, while 14 males (24.6%) were in non-survivor group; 33 females (76.7%) were in the survivor group, and 10 females (23.3%) were in the non-survivor group, respectively. In the present study, 54% of the patients had hypertension, 29% had ischemic heart disease, 27% had chronic kidney disease, and 24% had obstructive airway disease. The most frequent comorbidity in both groups was hypertension (54%), followed by ischemic heart disease (29%) and chronic kidney disease (27%). Comparison of the range of glycemic gap between survivors and non-survivors is shown in Table 2. Mean glycemic gap among survivors and non-survivors was 67.8 ± 53.4 and 97.3 ± 48.0 , respectively, showing that non-survivors had a higher mean glycemic gap than survivors, with statistical significance. (p -value=0.018). Among the various clinical and laboratory parameters, heart rate, random blood sugar (RBS), HbA1c, A1c-derived average blood sugar (ADAG), glycemic gap, serum sodium, serum creatinine, hematocrit,

white blood cell (WBC) count, and APACHE II score were higher among non-survivors than survivors, except for mean arterial pressure (MAP), which was lower in non-survivors than survivors. Of the various parameters, MAP (p -value=0.039), APACHE II score (p -value=<0.001), and glycemic gap (0.018) were all statistically significant between the two groups.

The glycemic gap differed notably between survivors and non-survivors. Non-survivors had a median glycemic gap of 60 mg/dL (interquartile range [IQR]: 45–75), whereas survivors had a median of 40 mg/dL (IQR 28–55). The median difference between groups was 20 mg/dL (95% CI 10–30 mg/dL), which was statistically significant (Mann–Whitney U test, p -value=0.002). These findings indicate a higher glycemic gap among patients who did not survive, supporting its potential association with adverse outcomes in critically ill patients. The ROC curve was plotted to calculate the glycemic gap cut-off for predicting mortality in critically ill diabetic patients. Glycemic gap cut-off was 56 mg/dL with a sensitivity and specificity of 79.2% and 60.5%, respectively. Glycemic gap was categorized into 4 groups, and the number of survivors and non-survivors in each group was studied. As shown in Table 3, patients with lower glycemic gaps had a higher rate of survival than patients with higher glycemic gaps, showing that higher glycemic gaps were associated with a higher mortality rate. For predicting mortality in ICU patients, the ROC curve was plotted for the APACHE II score and the glycemic parameters.

The area under the curve (AUC) was 0.672 (95% CI: 0.570–0.762, p -value=0.0028), indicating a fair discriminatory ability. The optimal cutoff value for the glycemic gap was >56 mg/dL, which yielded a sensitivity of 79.2% (95% CI: 57.8–92.9) and a specificity of 60.5% (95% CI: 48.6–71.6). The positive predictive value (+PV) was 38.8% (95% CI: 25.2–53.8), while the negative predictive value (–PV) was 90.2% (95% CI: 78.6–96.7).

Table 1 Comparison of clinical and laboratory parameters between survivors and non-survivors

Parameter	Survivors (n=76) Mean±S.D.	Non-survivors (n=24) Mean±S.D.	p-value
Age (years)	64.2±12.3	60.9±13.2	0.260
Heart rate (beats/min)	97.4±17.9	98.3±20.8	0.852
Mean arterial pressure (mmHg)	100.5±27.6	87.5±19.0	0.039*
Blood glucose at admission (mg/dL)	230.1±110.1	246.3±120.9	0.540
HbA1c (%)	9.1±2.6	9.6±2.5	0.457
ADAG (mg/dL)	218.3±77.4	228.3±71.0	0.573
Glycemic gap (mg/dL)	67.8±53.4	97.3±48.0	0.018*
Serum sodium (mmol/L)	131.7±8.5	132.9±8.7	0.539
Serum potassium (mmol/L)	4.6±1.0	4.6±1.2	0.932
Serum creatinine (mg/dL)	2.2±1.9	3.3±3.2	0.143
Hematocrit (%)	33.1±6.7	34.0±7.1	0.585
WBC count (/mm ³)	13,075.8±6,129.3	16,072.7±9,596.2	0.082
pH	7.4±0.1	7.3±0.1	0.102
APACHE II score	16.2±6.6	22.2±5.7	<0.001*
Sepsis, n (%)	40 (81.6%)	9 (18.4%)	0.244
Cardiovascular disease, n (%)	10 (71.4%)	4 (28.6%)	0.738
Respiratory disease, n (%)	9 (69.2%)	4 (30.8%)	0.506
Neurological disorders, n (%)	8 (80.0%)	2 (20.0%)	1.000
Renal failure, n (%)	3 (50.0%)	3 (50.0%)	0.148
Malignancy, n (%)	4 (100.0%)	0 (0.0%)	0.570
Liver disease, n (%)	2 (66.7%)	1 (33.3%)	0.565

Values are mean±S.D. or n (%). Independent t-test and Chi-square/Fisher's exact test were used as appropriate. *p-value<0.05 denotes statistical significance. HbA1c=hemoglobin A1c, ADAG=A1c-derived average glucose, WBC=white blood cell, APACHE II=acute physiology and chronic health evaluation II, S.D.=standard deviation

Table 2 Association of glycemic gap categories with mortality

Glycemic Gap (mg/dL)	Survivors (n=76), n (%)	Non-survivors (n=24), n (%)	Overall association (χ^2 test)
<0	2 (100.0)	0 (0.0)	0.023
1–40	38 (88.4)	5 (11.6)	
41–80	8 (80.0)	2 (20.0)	
81–120	13 (56.5)	10 (43.5)	

Table 3 Receiver operating characteristic curve analysis for various glucose parameters and apache II score

Parameter	AUC	95% CI	p-value
APACHE II score	0.779	0.685–0.856	<0.001
Glycemic gap	0.672	0.570–0.762	<0.001
HbA1c	0.556	0.453–0.655	0.276
Admission blood sugar	0.539	0.436–0.639	0.450

AUC=area under the curve, 95% CI=95% confidence interval, APACHE II=Acute Physiology and Chronic Health Evaluation II, HbA1c=hemoglobin A1c

APACHE II score (AUC 0.779) was the best predictor of mortality in critically ill patients, followed by the glycemic gap (AUC 0.672) (Figures 1 and 2) (Table 3). Among glycemic indices, glycemic gap had better discriminative power in predicting mortality than HbA1c and admission blood sugar, with AUC being 0.672, 0.556, and 0.539, respectively. The Kaplan Meier survival curve was used to analyze the probability of survival in people with glycemic gaps of 56 mg/dL and higher. Glycemic gaps of 56 mg/dL and higher were associated with a statistically significant difference in in-hospital mortality (Log rank $p=0.005$) (Figure 3). However, because in-hospital mortality is a discrete event without censoring, the incremental analytical value of the Kaplan–Meier curve is limited to descriptive visualization of time-to-death patterns rather than inferential prediction. The survival plot is exploratory and presented only for temporal visualization.

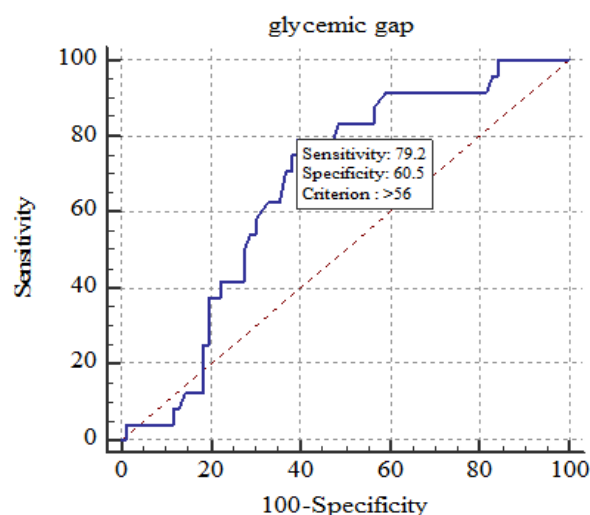
Patients with Glycemic gaps >56 mg/dL had a higher mortality rate (38%) than patients with glycemic gaps <56 mg/dL (5%), showing a statistically significant relationship between the glycemic gap and mortality. (0.01 p -value). Individuals with a glycemic gap >56 mg/dL had a higher mortality rate (p -value 0.001), risk of developing shock (p -value 0.102), increased requirement for ventilator support (p -value 0.116), and a higher likelihood of needing dialysis (p -value 0.03) (Table 4). The glycemic gap was statistically significant for predicting mortality, the likelihood of developing AKI, and the requirement for dialysis.

On multivariate logistic regression adjusting for age, sex, APACHE II score, admission diagnosis, baseline HbA1c, pre-ICU antihyperglycemic therapy, chronic kidney disease, steroid use, sepsis/infection status, and mechanical ventilation at admission, glycemic gap was independently associated with ICU mortality (adjusted OR 1.04 per mg/dL increase, 95% CI 1.02–1.06, p -value <0.001). Other independent predictors of mortality included APACHE

II score (OR 1.09, 95% CI 1.05–1.13, p -value <0.001), shock/inotrope support (OR 2.45, 95% CI 1.55–3.88, p -value <0.001), ventilator support/ARF (OR 2.12, 95% CI 1.30–3.45, p -value=0.002), and age (OR 1.03 per year, 95% CI 1.01–1.06, p -value=0.02). Sensitivity analyses yielded similar results, confirming the robustness of the findings.

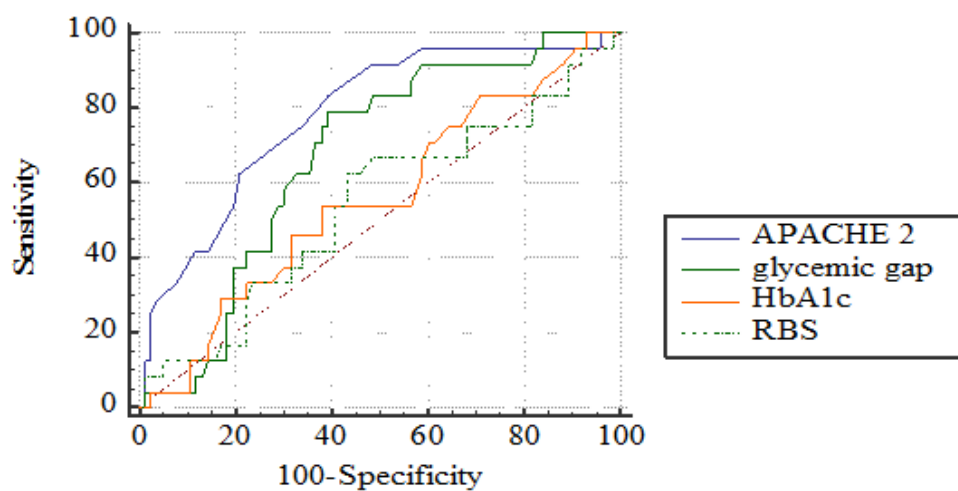
In the multivariable model, ADAG remained statistically significant (adjusted OR 1.04 per mg/dL; 95% CI). Although VIF values were <5 , partial collinearity with HbA1c cannot be fully excluded and may contribute to the magnitude of the observed association (Table 5).

Although the minimum recommended event-per-variable (EPV) ratio of 10 could not be achieved for all covariates, the authors took several steps to reduce the risk of model overfitting. Multivariable analysis was restricted to clinically relevant covariates selected a priori rather than through data-driven selection, and multicollinearity was assessed prior to model entry to avoid redundant predictors.



ROC=receiver operating characteristic

Figure 1 ROC curve for glycemic gap in predicting mortality



ROC=receiver operating characteristic, HbA1c=hemoglobin A1c, RBS=random blood sugar, APACHE II=acute physiology and chronic health evaluation II

Figure 2 ROC curve for various glucose parameters like HbA1c, RBS (admission glucose level), glycemic gap, and APACHE II score in predicting mortality

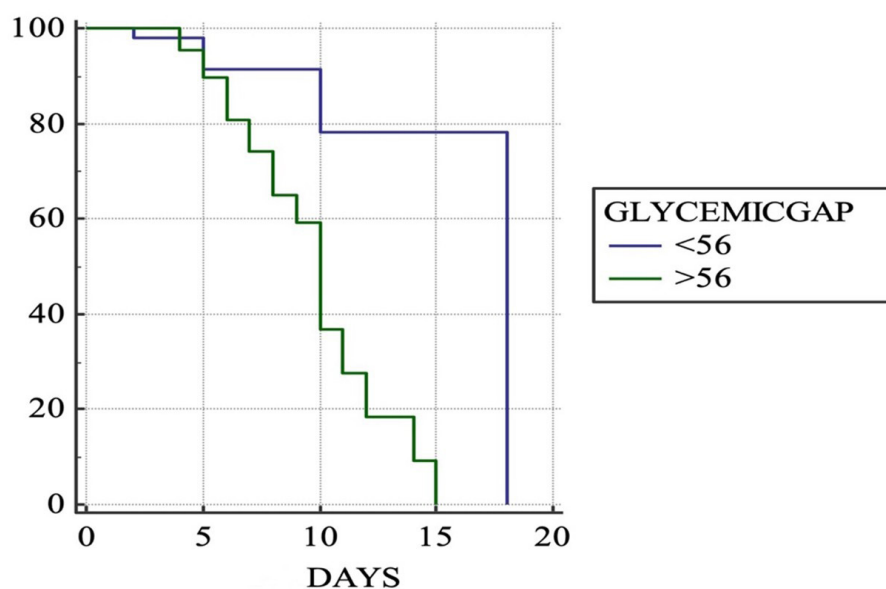


Figure 3 Kaplan Meier survival curve of the glycemic gap

Table 4 Comparison of adverse outcomes by glycemic gap category

Adverse outcome	Glycemic gap <56, n (%)	Glycemic gap >56, n (%)	p-value
Mortality	5 (5)	19 (38)	<0.001
MODS	22 (43.1)	17 (34.7)	0.418
Shock	16 (31.4)	24 (49.0)	0.102
AKI / Need of dialysis	21 (41.2)	31 (63.3)	0.030
Need of ventilator	22 (43.1)	29 (59.2)	0.116

MODS=multiple organ dysfunction syndrome, AKI=acute kidney injury

Table 5 Multivariable logistic regression analysis of factors associated with in-hospital mortality

Predictor	Adjusted OR	95% CI	p-value
Glycemic gap (per mg/dL)	1.04	1.02–1.06	<0.001
ADAG (per 1 mg/dL)	1.009	1.002–1.016	0.0177
Age (per year)	1.03	1.01–1.06	0.02
Male gender	1.25	0.80–1.95	0.33
APACHE II score	1.09	1.05–1.13	<0.001
Diabetes mellitus	1.10	0.70–1.72	0.65
Chronic kidney disease	1.68	1.02–2.78	0.04
Shock / inotrope support	2.45	1.55–3.88	<0.001
Ventilator support / ARF	2.12	1.30–3.45	0.002
HbA1c (%)	1.05	0.95–1.16	0.35
MAP (mmHg)	0.98	0.96–1.01	0.18

ADAG=A1C derived glucose, WBC=white blood corpuscles, APACHE=acute physiology and chronic health evaluation, OR=odds ratio, ARF=acute respiratory failure, MAP=mean arterial pressure

Discussion

Hospitalized patients with stress-induced hyperglycemia demonstrate increased mortality. This condition arises from the surge of counter-regulatory hormones and cytokines that enhance gluconeogenesis and impair insulin sensitivity. As many diabetic patients have historically high blood glucose levels, measuring admission glucose in these individuals may not correlate with stress levels. To counter this fallacy, the glycemic gap was calculated, which subtracts baseline hyperglycemia from admission blood sugar, yielding actual stress-induced hyperglycemia. Studies have shown that stress-induced

hyperglycemia could predict outcomes in critically ill patients because the severity of SIH correlates with disease severity.

The study included 100 patients admitted to the medical ICU. Baseline data obtained were age, gender, comorbidities, primary diagnosis, APACHE II score, and glycemic gap. The patients were followed up till discharge or death, and negative outcomes like MODS, shock, need for mechanical ventilator support, and AKI were recorded. The majority of patients belonged to the age group 51–70 years. The mean age±standard deviation between survivors and non-survivors was 64.2±12.3 and 60.9±13.2, respectively. A similar observation was made in a study by Donagaon et

al.⁵. However, in our study, the mean age among survivors and non-survivors was comparable, with no statistical significance. In this study, among 57 male patients, 43 (75.4%) were in the survivor group, and 14 (24.6%) were in the non-survivor group. Of 43 females, 33 (76.7%) were in the survivor group and 10 (23.3%) the non-survivor group. There was no statistically significant difference in gender between the two groups. This was consistent with another study by Wen-I Liao et al.⁶ that had a large sample size and found that out of 87 patients who died, 47 (54%) were men and 40 (45%) were women. Similar results were seen in another study by Ran Lou et al.⁷, where 101 (52.6%) of the 192 non-survivors were men and 83 (43%) were women, respectively. The comorbidities noted in our study included hypertension, ischemic heart disease, chronic kidney disease, obstructive airway disease, cerebrovascular accident, and chronic liver disease. Hypertension (56%) was the most common comorbidity, followed by ischemic heart disease (29%), renal disease (27%), and obstructive airway disease (24%). A similar observation was made in a study done by Ran Lou et al.⁷, where cardiac and vascular disease (77%), including hypertension, was the most common comorbidity. The primary diagnosis included sepsis (49%), cardiovascular disorders (14%), respiratory disease (13%), neurological disorders (10%), renal failure (6%), malignancy (4%), and liver disease (3%).

In our study, 49% of the 100 ICU patients had sepsis as their primary diagnosis, which was consistent with a study by Wen-I Liao et al.⁶, where 57.5% of all patients had an infection. Glycemic gap as a predictor of outcome in critically ill patients was studied, and the efficacy of the different glucose parameters in predicting mortality was evaluated. The mean glycemic gap in our study between survivors and non-survivors was 67.8±53.4 and 97.3±48.0, with a statistically significant p-value of 0.018. The glycemic gap cutoff determined using the ROC curve was found to be 56 mg/dL with a sensitivity and specificity of 79.2% and

60.5%, respectively. Similar findings were made in a study by Wen-I Liao et al.⁶, who found that the mean glycemic gap between survivors and non-survivors was 57.1 and 131.2, respectively, and that 80 mg/dL was the optimum cutoff for the glycemic gap to predict mortality, with sensitivity and specificity of 64.0% and 68.8%, respectively. The Kaplan-Meier survival curve for predicting survival probability shows that a glycemic gap >56 mg/dL was associated with a significantly shorter survival than a glycemic gap < 56 mg/d. Patients with a higher glycemic gap tended to have higher mortality than those with a lower glycemic gap, and the ICU mortality rate increased markedly when the glycemic gap exceeded 56mg/dL. This was inconsistent with a study by Wen-I Liao et al.⁶. The glycemic gap is a better marker than admission glucose, HbA1c, and the other variables used to measure stress-induced hyperglycemia because it eliminates the impact of persistent baseline hyperglycemia. The discriminative power of the glycemic gap was higher than that of admission blood glucose and HbA1c, with AUCs of 0.672 (95% CI: 0.570 to 0.762), 0.556 (95% CI: 0.453 to 0.655), and 0.539 (95% CI: 0.436 to 0.639), respectively. This is consistent with a study by Wen-I Liao et al.⁶, where the discriminative power of the glycemic gap for predicting ICU mortality was greater than that of admission glucose and Hba1c with AUCs of 0.703 (95% CI: 0.64–0.77), 0.673 (95% CI: 0.61–0.74), and respectively 0.467 (95% CI: 0.40–0.54). Another study by Philip et al.⁸ also showed that the discriminative power of the glycemic gap (AUC 0.77) in predicting ICU mortality was greater than that of the admission glucose (AUC 0.73).

Previous studies by Wen-I Liao et al.⁶ and Donagaon et al.⁵ showed that a higher glycemic gap was associated with an increased risk of adverse outcomes like MODS, AKI, developing shock, need of inotropic support, need of mechanical ventilator support, and need of dialysis. In the present study, patients with a glycemic gap >56 mg/dL were associated with increased risk of developing shock

49.0% vs 31.4%), need of ventilator support (59.2% vs 43.1%), and risk of developing AKI/need of dialysis (63.3% vs 41.2%). A similar observation was made in a study by Wen-I Liao et al.⁶, patients with a glycemic gap >80 mg/dL were associated with an increased risk of developing shock (39.5% vs 25.9%), risk of developing AKI (30.5% vs 17.4%), and weaning failure (12.1% vs 9.1%).

The mean duration of ICU stays, and hospital stay between patients with glycemic gap < 56 and glycemic gap >56 mg/dL was 5.9±3.3, 12.0±5.0, and 6.6±S.D. 2.9, 12.1±4.6, respectively, which was not statistically significant. In a similar study conducted by Wen-I Liao et al.⁶, the mean duration of ICU and hospital stays in patients with higher and lower glycemic gaps were 15.9±20 and 17.6±20, and 25.5±26.0 and 25.4±22.6, respectively.

Several scoring systems, including APACHE II, SAPS, SOFA, and MPM, are used in intensive care units to manage and prognosticate on patients. It has been demonstrated in numerous earlier studies^{9,10} that the APACHE II score was a more reliable scoring method for predicting outcomes in critically ill patients. The APACHE II score was utilized in the current study as a standard scoring system for predicting mortality, and it was compared to a few glycemic markers. According to this study, the APACHE-II score (AUC 0.779) was the best score for predicting mortality, followed by the glycemic gap score (AUC 0.672). Among glycemic indicators, glycemic gap had a better discriminative power than HbA1c and admission blood glucose with AUC of 0.672 (95% CI 0.57 to 0.76), 0.556 (95% CI 0.45 to 0.65), and 0.539 (95% CI 0.44 to 0.64), respectively. Another study by Farid Fawzy et al.¹¹ showed that a higher glycemic gap was significantly associated with an increased ICU mortality, and the APACHE II score was a better predictor of ICU mortality in critically ill patients. None of the scores take glucose as a value while predicting the risk of mortality.

Although the discriminative performance (AUC=0.67) is inferior to APACHE II, the glycemic gap is a useful marker due to its low cost and widespread availability. Future studies with larger multicenter cohorts are needed to determine whether incorporating this biomarker into existing prognostic models could improve clinical decision-making. Glycemic gap shows a modest association with disease severity and may serve as a supplementary indicator alongside established scoring systems.

The studies, including Liao et al. (2015) and Lou et al. (2021), have demonstrated the prognostic value of the glycemic gap. Specifically, there is a lack of data on glycemic gap as a prognostic marker in South Asian/Indian T2DM patients who have distinct metabolic profiles, stress glycemic response patterns, and higher baseline HbA1c compared to Western and East Asian cohorts. The study also reports the relationship between glycemic gap and non-mortality outcomes (mechanical ventilation, shock, and acute kidney injury), which are not uniformly reported in prior studies^{6,7}.

The present study has certain limitations. It was conducted in a single tertiary-care center with a relatively small sample size of 100 patients, which may limit the power for extensive multivariable adjustment and the generalizability of findings. However, this exploratory design was intended to generate preliminary data on the prognostic role of the glycemic gap in an Indian ICU setting, where limited data currently exist. Despite these constraints, the study demonstrated consistent associations between glycemic gap and adverse clinical outcomes, suggesting potential clinical relevance that warrants confirmation in larger, multicenter cohorts.

Despite these limitations, the present study has several strengths. It is among the few studies from South India to evaluate the glycemic gap as a prognostic marker among critically ill patients. The study utilized standardized definitions, validated severity scoring (APACHE II), and

quality-controlled biochemical assays performed in an accredited laboratory, ensuring methodological rigor. Additionally, by comparing glycemic gap with APACHE II and examining its association with specific organ dysfunctions, such as shock, ventilator requirement, and acute kidney injury, the study provides novel, contextually relevant insights that can inform future research and clinical risk stratification in Indian ICU settings.

This study provides new data from South Indian critically ill patients, highlighting the prognostic relevance of the glycemic gap in a population that has been underrepresented in prior research. Its comparison with APACHE II and association with specific organ dysfunctions enhance its contextual and clinical significance.

This score could be of vital use in predicting mortality, as elevated blood glucose levels have a potential role in the survival of critically ill patients. However, further studies are required to consider the glycemic marker also in predicting outcomes in critically ill patients. Although the glycemic gap demonstrated significant associations with adverse clinical outcomes, the observed discriminatory ability was modest, and causality cannot be inferred. Therefore, the present findings should be regarded as supportive of prior evidence and hypothesis-generating, warranting further validation in larger, multicenter cohorts.

Conclusion

In this single-center study from South India, a higher glycemic gap was associated with an increased risk of adverse outcomes, including shock, need for mechanical ventilation, and acute kidney injury in critically ill patients. Although its discriminatory performance was modest, our findings align with previous research and underscore the potential relevance of glycemic variability in critical illness. The glycemic gap may serve as a supplementary indicator of disease severity when used alongside established prognostic scoring systems.

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