

Research Article

The Effect of Multiple Glycemic Parameters on Mortality and Clinical Outcomes in Critically Ill Patients in Intensive Care Unit

Wasihun Zerfu Zewde^{1,*} , Amare Gulilat Mamo¹ , Helina Yohannes Afework² , Mahlet Mitiku Desalegn¹ , Ermiyas Berehanu Hayle¹ , Zewdu Abadi Tsegay³ , Mehariw Wondim Netsere¹ , Amir Muhidin Abraham⁴ , Yeabtsega Amlaku Asres³ 

¹Departement of Internal Medicine, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

²School of Medicine, Jimma University, Jimma, Ethiopia

³School of Medicine, Addis Ababa University, Addis Ababa, Ethiopia

⁴Department of Emergency Medicine, Adama Hospital Medical College, Adama, Ethiopia

Abstract

Background: Dysglycemia is frequently encountered in the ICU and it includes hyperglycemia, hypoglycemia and glycemic variability which are associated with increased rate of mortality and morbidity. Hyperglycemia is the most frequent among the components of dysglycemia and its prevalence is 40-90%. The prevalence and outcome of multiple glycemic parameters in the ICU has not been described in Ethiopia. Objectives: The aim of the study is to describe the effect of multiple glycemic parameters on intensive care unit mortality and clinical outcomes in selected tertiary hospitals. Methods: An institution based cross-sectional study was conducted by using systematic random sampling. Data was collected from patient cards and was entered using Epi Info 7.2. Data analysis was done using SPSS 27.0. Descriptive statistics was used to summarize the data. Associations between variables were measured with chi square and Mann Whitney U test. Multivariable logistic regression was used to identify predictors of mortality and test the association of multiple glycemic parameters and mortality. Odds ratios with 95% confidence intervals were calculated, and a p-value <0.05 was considered to declare significance Result: The study included 392 patient records, with a median age of 38 years [IQR 28 – 56]. About 53% of patients were females. The prevalence of hyperglycemia, hypoglycemia and high glycemic variability was 90.3%, 16.3% and 19.4% respectively. Hypoglycemia was significantly associated with mortality (AOR 2.98, p < .05). Patients with hyperglycemia and hypoglycemia had significantly longer lengths of stay and durations of mechanical ventilation. High glycemic variability was not significantly associated with mortality, length of stay or duration of mechanical ventilation. Conclusion: Dysglycemia is very prevalent among patients admitted in the ICU and hypoglycemia may be associated with ICU mortality and adverse clinical outcomes.

Keywords

Critical Illness, Dysglycemia, Stress Hyperglycemia, Hypoglycemia, Glycemic Variability, Mortality

*Corresponding author: wasezzewde@gmail.com (Wasihun Zerfu Zewde)

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1. Introduction

An intensive care unit (ICU) is a specialized unit of a hospital reserved for patients with serious and life-threatening illnesses that call for careful monitoring, specialized care, and the use of various high-technology equipment and medications to preserve normal physiologic function in humans. ICUs are advanced facilities with the most cutting-edge medical equipment and trained staff in the majority of developed nations. Caring for the critically ill patients is a challenge in developing countries, where health needs often outstrip available resources [1].

Critically ill patients frequently have stress hyperglycemia (also called critical illness hyperglycemia). It is reported prevalence in ICU ranges from 40% to 90% depending on the cut-off value used [2]. The American diabetic association (ADA) defines in-hospital hyperglycemia as any blood glucose (BG) value above 140 mg/dl [3]. Although the primary etiology of stress hyperglycemia is the acute metabolic and hormonal changes associated with the response to injury and stress, there are several factors that can cause hyperglycemia in these groups of patients. Some of the causes include use of vasopressors and glucocorticoids. While it is known that patients with known diabetes are at risk for developing hyperglycemia while critically ill, people who have never been diagnosed with diabetes are actually the ones who are most at risk [4]. Poor outcomes like mortality and increased length of ICU & hospital stay are associated with stress hyperglycemia. Although whether hyperglycemia is a cause of increased hospital mortality or just an epiphenomenon was an issue of controversy, there are several studies that have shown the association was independent of disease severity [2, 5, 6].

Hospitalized individuals with hyperglycemia fall into three categories [4]. Patients with known history of diabetes, patients with unrecognized diabetes and patients with stress hyperglycemia. Unrecognized diabetes and stress hyperglycemia are differentiated using hemoglobin A1c (HbA1c). If the patient's HbA1c is less than 6.5%, the patient has a stress hyperglycemia. But if the patient's HbA1c is 6.5% or more, the patient has unrecognized diabetes [7].

Hypoglycemia is defined as having one or more BG values less than 70 mg/dL according to ADA. This value is recognized as a threshold for neuroendocrine responses to falling glucose in people without diabetes. A blood glucose concentration <54 mg/dL is the threshold at which neuroglycopenic symptoms begin to occur [3]. Although the severity of hypoglycemia may be just a marker of the severity of illness, hypoglycemia itself might be harmful for acutely ill patients. For example, hypoglycemia might be biologically toxic by inducing neuroglycopenia, increasing the systemic inflammatory response, causing cerebral vasodilatation, impairing sympathetic nervous system responsiveness, inhibiting the corticosteroid response to stress, or by mechanisms that have yet to be determined [8].

Dysglycemia is defined by hyperglycemia, hypoglycemia and high glycemic variability & is associated with poor outcomes. Previously the focus of glycemia in critically ill patients was on controlling hyperglycemia and hypoglycemia, but recently glycemic variability (GV) has entered the picture as one of the factors that affects outcomes in this group of patients [5, 9].

Glycemic variability refers to swings in blood glucose levels. Best methods to measure GV are standard deviation (SD) and coefficient of variance (CV). Although the underlying mechanisms are not completely understood, increasing evidence indicates that fluctuations in blood glucose are associated with factors associated with the pathogenesis of vascular damage like endothelial dysfunction, inflammation and oxidative stress. By these proposed mechanisms high GV contributes to morbidity and mortality of critically ill patients [9, 10].

Determining the patterns of dysglycemia and associated clinical outcomes in critically ill patients would help develop the necessary attitude towards the problem among physicians. Identifying which patients are at high risk for dysglycemia associated morbidity and mortality will help clinicians by guiding their decision-making process. Factors associated with prolonged length of stay and mortality in the ICU are also crucial in developing quality improvement initiatives targeting critically ill patients. The findings of this study can be of valuable input for health care authorities in understanding, prioritizing and planning glycemic control related problems and developing the capacity to mitigate the impacts of morbidity and mortality of critically ill patients. The magnitude and impacts of this problem can serve as possible evidence for the proper allocation of resources in critical care settings. The findings of this study can also emphasize the need for adopting clinical management guidelines for optimizing glycemic control of critically ill patients in the ICU. This study will be one of the first in exploring glycemic control problems among critically ill patients in our country. Apart from promoting evidence-based practice, this study can also serve as a baseline for conducting further studies in this area.

2. Materials and Methods

A hospital based cross-sectional study was conducted in St Paul's hospital millennium medical college (SPHMMC) and Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, Ethiopia. SPHMMC and TASH are the two largest tertiary hospitals in the country. SPHMMC has more than 700 beds, The College sees an average of 1200 emergency and outpatient clients daily [11]. TASH has a total bed capacity of approximately 800 beds and provides specialty services for nearly half a million patients per year coming from every corner of the country. The ICU setup of SPHMMC has 2

separate ICUs and 14 beds. According to data reported from the hospital's HMIS office the ICU has an average monthly admission of 26 patients and an average yearly admission of 312 patients. The ICU setup of TASH has a total of 12 beds. About 180–200 patients receive invasive mechanical ventilation per year in the intensive care unit [12].

Selected critically ill adult (≥ 18 years of age) patients admitted to SPHMMC and TASH intensive care units from April 1, 2022 to March 31, 2023 were included in the study. Patients with the diagnosis of Diabetic Ketoacidosis or Hyperglycemic Hyperosmolar Syndrome on ICU admission and patients known to be pregnant or lactating were excluded from the study. A total of 813 patient records were screened for inclusion, out of which 397 had incomplete data, and 42 were excluded based on predefined exclusion criteria. 392 patient records were included in the final analysis.

Data was collected from patients' cards and ICU follow up sheets using a data collection checklist. Blood glucose measurements was grouped and GV was reported as coefficient of variance calculated from each measurement. High glycemic variability was defined as coefficient of variance of greater than 36% calculated from the patient's total blood glucose measurements [13].

Blood glucose measurements were grouped into 5 using 4 cutoff values per ADA guidelines. The first was 54 mg/dL which defines level 2 hypoglycemia. The second was 70 mg/dL which defines hypoglycemia. The third was 140 mg/dL which defines in-hospital hyperglycemia. The fourth was 180 mg/dL which defines uncontrolled hyperglycemia and is the upper limit of the glycemic target in the ICU [3].

Age-combined Charlson comorbidity index (CCI) was used as a representation of patients' comorbidities [14–16]. Norepinephrine equivalent doses were used to calculate cumulative

doses of vasopressors [17]. Hydrocortisone equivalent doses were used to calculate cumulative doses of steroids [18, 19].

Data entry was done using Epi Info version 7.2 and exported to Statistical Package for the Social Sciences (SPSS) version 27.0 for further data analysis. Descriptive analysis was carried out for all variables. Categorical variables were recorded as percentages and frequency and were compared by chi square test. Continuous variables were recorded as median and interquartile range and were compared by Mann Whitney U test. Bivariate analysis between dependent and independent variables was performed using binary logistic regression. Multivariate logistic regression was used to identify predictors of mortality and test the association of glycemic parameters and mortality. Mann Whitney U was used to assess the relation between multiple glycemic parameters and increased ICU length of stay and increased duration on MV. If the p value was <0.05 , then the difference between various parameters was considered statistically significant. Results were presented as tables, graphs and charts.

3. Results

3.1. Demographic Characteristics

The median [IQR] age of patients included in this study is 38 years [IQR = 28 – 56] and the age group 18 to 40 years constitute 55.6% (218) of the sample. The sex distribution was 47.4% (186) females and 52.6% (206) males. The permanent area of residence for 62.84% (246) of patients is Addis Ababa, followed by Oromia (24.5% (96)) and Amhara (4.6% [18]) regions. (Table 1).

Table 1. Demographic characteristics of the sample.

Characteristics	Overall	ICU Mortality		p value
		Dead	Alive	
Study Participants	392 (100.0)	138 (35.2)	254 (64.8)	NA
Age, M (IQR)	38 (28 - 56)	38 (28 - 54)	38 (30 - 56)	.653
Age Group (yrs.)				
18–30	124 (31.6)	42 (33.9)	82 (66.1)	.008
31–40	94 (24.0)	30 (31.9)	64 (68.1)	
41–50	54 (13.8)	28 (51.9)	26 (48.1)	
51–60	44 (11.2)	14 (31.8)	30 (68.2)	
61–70	48 (12.2)	10 (20.8)	38 (79.2)	
71–80	20 (5.1)	8 (40.0)	12 (60.0)	
> 80	8 (2.0)	6 (75.0)	2 (25.0)	
Sex				

Characteristics	Overall	ICU Mortality		p value
		Dead	Alive	
Female	186 (47.4)	72 (38.7)	114 (61.3)	.161
Male	206 (52.6)	66 (32.0)	140 (68.0)	
Address				
Addis Ababa (city)	246 (62.8)	90 (36.6)	156 (63.4)	.01
Afar Region	2 (0.5)	0 (0.0)	2 (100.0)	
Amhara Region	18 (4.6)	12 (66.7)	6 (33.3)	
Oromia Region	96 (24.5)	24 (25.0)	72 (75.0)	
Southern Nations, Nationalities and Peoples	16 (4.1)	6 (37.5)	10 (62.5)	
Tigray Region	8 (2.0)	4 (50.0)	4 (50.0)	
Others	6 (1.5)	2 (33.3)	4 (66.7)	

*p values are for Pearson's Chi-square test of independence.

3.2. Clinical Characteristics

The most common comorbidities were hypertension (22.40% (88)), Chronic Heart Failure (12.8% (50)), HIV infection (10.2% (40)), Type 2 Diabetes Mellitus (9.7% (38)), chronic kidney disease (9.2% (36)) and malignancies (6.1%

(24)). The median age-combined CCI is 1 with IQR of 0-4 and 32.1% (126) of patients had an age-combined CCI score of 0. The commonest diagnosis made at or during the admission are hospital acquired infection (39.3% (154)), acute kidney injury (37.8% (148)), respiratory failure (26.5% (104)), shock (19.9% (78)), acute heart failure (10.2% (40)), and acute cerebral accidents (7.1% (28)). (Table 2).

Table 2. Diagnosis made during ICU admission and mortality.

Characteristics	Overall	ICU Mortality		p value*
		Dead	Alive	
Study Participants	392 (100.0)	138 (35.2)	254 (64.8)	NA
Acute Kidney Injury	148 (37.8)	64 (43.2)	84 (56.8)	.012
Acute Myocardial Infarction	8 (2.0)	2 (25.0)	6 (75.0)	.718
Acute Heart Failure	40 (10.2)	12 (30.0)	28 (70.0)	.601
Acute Cerebral accident	28 (7.1)	4 (14.3)	24 (85.7)	.022
Hospital Acquired Infections	154 (39.3)	60 (39.0)	94 (61.0)	.234
CNS Infections**	10 (2.6)	4 (40.0)	6 (60.0)	.746
Shock	78 (19.9)	44 (56.4)	34 (43.6)	<.001
Type of shock				
No Shock	314 (80.1)	94 (29.9)	220 (70.1)	<.001
Septic Shock	56 (14.3)	38 (67.9)	18 (32.1)	
Hypovolemic Shock	4 (1.0)	0 (0.0)	4 (100.0)	
Cardiogenic Shock	18 (4.6)	6 (33.3)	12 (66.7)	
Respiratory Failure	104 (26.5)	60 (57.7)	44 (42.3)	<.001

Characteristics	Overall	ICU Mortality		p value*
		Dead	Alive	
Acute Liver Failure	16 (4.1)	10 (62.5)	6 (37.5)	.03
Tuberculosis	22 (5.6)	12 (54.5)	10 (45.5)	.065
Venous thromboembolism	18 (4.6)	6 (33.3)	12 (66.7)	.865
Others	100 (25.5)	10 (10.0)	90 (90.0)	<.001

*p values are for Pearson's chi square test.
 ** CNS – Central nervous system.

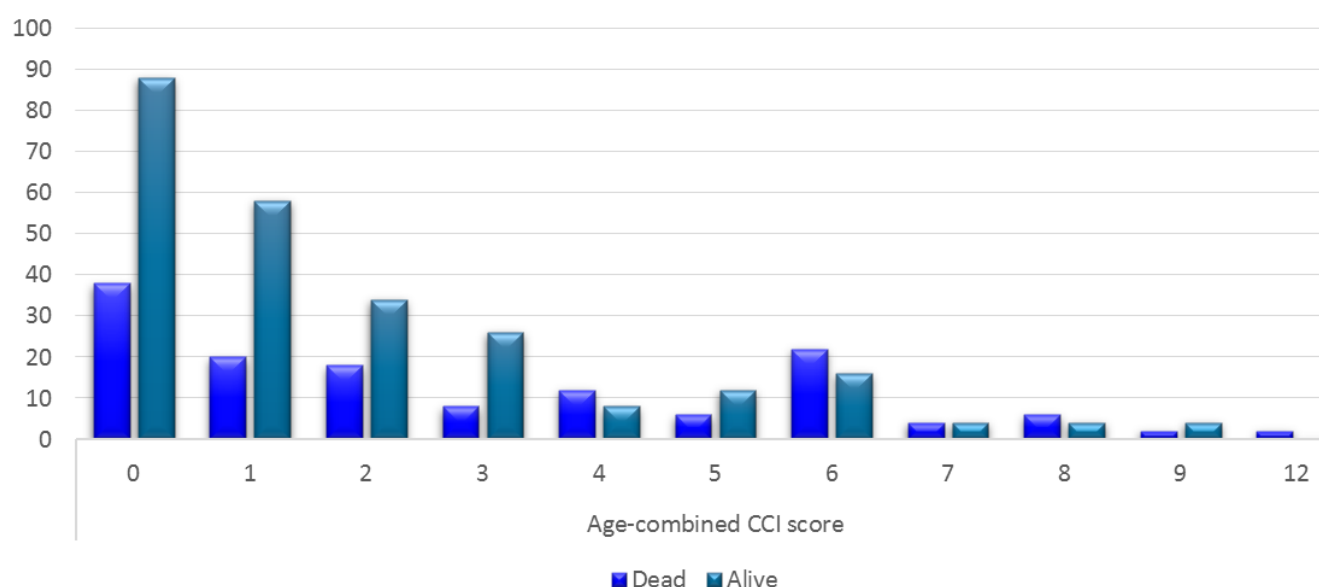


Figure 1. Age-combined CCI and ICU mortality.

3.3. Glycemic Parameters

The estimated prevalence of hyperglycemia in the sample was 90.3% (95% CI [86.9%, 92.9%]). The prevalence of hypoglycemia was 16.3% (95% CI [13%, 20.3%]) and the prevalence of high glucose variability was estimated to be

19.4 (95% CI [15.8%, 23.6%]). The Prevalence of hyperglycemia in non-diabetics was 89.6% (95% CI [56.9%, 92.4%]). Because of the limitation associated with the small subset of patients with HbA1C determined within the preceding 3 months (9.3%, 34) and even smaller number of patients who were not diabetic (29.4%, 10) the prevalence of stress hyperglycemia cannot be concluded.

Table 3. Glycemic Profiles, administered medications, age-combined CCI and ICU Mortality.

Characteristics	Overall	ICU Mortality		p value*
		Dead	Alive	
Age-combined CCI, M (IQR)	1 (0 - 4)	2 (0 - 6)	1 (0 - 3)	.001
Glycemic Profiles				
Stress Hyperglycemia	8 (2.0)	0 (0.0)	8 (100.0)	.055

Characteristics	Overall	ICU Mortality		p value*
		Dead	Alive	
Hyperglycemia	354 (90.3)	122 (34.5)	232 (65.5)	.371
Hypoglycemia	64 (16.3)	38 (59.4)	26 (40.6)	<.001
High Glycemic Variability	76 (19.4)	32 (42.1)	44 (57.9)	.161
Glycemic variability, M (IQR)	26.1 (19.8 - 32.7)	27.21 (21.2 - 35.6)	24.7 (19.1 - 30.5)	.009
Medications given in the ICU				
Use of insulin	66 (16.8)	16 (24.2)	50 (75.8)	.048
Mode of insulin				
None	326 (83.2)	122 (37.4)	204 (62.6)	.065
Subcutaneous	56 (14.3)	12 (21.4)	44 (78.6)	
Intravenous	10 (2.6)	4 (40.0)	6 (60.0)	
Use of any glucocorticoids	78 (19.9)	42 (53.8)	36 (46.2)	<.001
Use of any Vasopressors	122 (31.1)	86 (70.5)	36 (29.5)	<.001
Dose of Steroids. (mg), M (IQR) **	800 (360 - 1280)	640 (250 - 853)	1085 (640 - 1800)	.001
Dose of Vasopressors (mg), M (IQR) ***	42.6 (5 - 93)	52 (10 - 166)	15 (5 - 53)	.002
Dose of Insulin, M (IQR)	60 (19 - 210)	146.5 (13.5 - 225.5)	49 (19 - 187)	.719

Abbreviations: CCI – Charlson Comorbidity Index, ICU – Intensive Care Unit, M (IQR) – Median (interquartile range).

*p values are for Pearson's Chi-square test of independence, except: Mann-Whitney U test for Doses of Steroid, vasopressor, insulin, glycemic variability, and age-combined CCI.

** Dose of steroids are in hydrocortisone equivalent doses.

*** Doses of vasopressors are in noradrenaline equivalent doses.

3.4. Associations of Glycemic Parameters and ICU Mortality

The overall prevalence ICU mortality in our study was 35.2% (95% CI [30.6%, 40.1%]). Chi-square test of independence was performed to examine the relation between categorical independent variables and ICU mortality. The result revealed that age group, acute kidney injury, acute cerebral accidents, Shock, Respiratory failure, Acute liver failure, Hypoglycemia, Use of insulin, Use of glucocorticoids, and Use of vasopressor were significantly associated with mortality ($p < 0.05$).

Crude associations for all independent variables with ICU mortality was done by using bivariable logistic regression. Variables with p values of less than 0.2 in the bivariate logistic regression analysis were selected for multivariable logistic regression analysis. Subsequently age groups, age-combined

CCI, acute kidney injury, acute cerebral accidents, shock, respiratory failure, acute liver failure, hypoglycemia, glycemic variability, use of insulin, use of vasopressors, and use of glucocorticoids were candidates for the final model. After adjusting for potential confounders only age-combined CCI, respiratory failure, hypoglycemia, use of insulin and use of vasopressors were significantly associated with ICU mortality among the study population.

The logistic regression analysis revealed that hypoglycemia had a significant positive effect on the likelihood of mortality. The odds ratio for hypoglycemia was 2.98, indicating that for every one record of hypoglycemia ICU patients have 3-fold increased odds of dying in reference to patients with no hypoglycemia. After controlling for age groups, diagnoses made during the ICU stay, Shock, glycemic variability, age combined CCI, use of insulin, use of glucocorticoids, and use of vasopressors, the relationship between hypoglycemia and mortality remained statistically significant. ($B = 1.10$, $SE =$

0.41, Wald $\chi^2(df) = 7.18 (1)$, $p < .05$, AOR = 2.98, 95% CI [1.34, 6.62]).

The logistic regression analysis also revealed a statistically significant association between insulin use and mortality ($B = -1.64$, $SE = 0.464$, Wald = 12.474, $df = 1$, $p < 0.001$). Patients who used insulin had a lower likelihood of mortality compared to those who did not use insulin. A Spearman's correlation

was conducted to evaluate the relationship between hyperglycemia and BG between 140-180 mg/dL with dose of insulin. There was a significant positive relationship between hyperglycemia and dose of insulin, ($r_s = 0.379$, $p = < .001$) and there was a significant positive relationship between BG between 140-180 mg/dL and dose of insulin, ($r_s = 0.168$, $p = < 0.001$).

Table 4. Multivariable Binary Logistic Regression analysis of 392 patients for predictors of ICU mortality.

Parameter	COR (95%CI)	AOR (95%CI)	p value
Age Groups (years)			
18-30	1	1	
31-40	0.92 (0.52, 1.62)	0.79 (0.39, 1.62)	0.515
41-50	2.103 (1.10, 4.03)	2.31 (0.95, 5.64)	0.066
51-60	0.91 (0.44, 1.90)	0.64 (0.22, 1.85)	0.408
61-70	0.51 (0.23, 1.13)	0.17 (0.05, 0.54)	0.003
71-80	1.30 (0.49, 3.43)	1.24 (0.33, 4.63)	0.747
> 80	5.86 (1.13, 30.28)	1.09 (0.14, 8.29)	0.935
Age-combined CCI	1.17 (1.08, 1.27)	1.30 (1.14, 1.47)	<0.001
Acute Kidney Injury	1.75 (1.14, 2.68)	1.15 (0.62, 2.11)	0.658
Acute Cerebral Accident	0.286 (0.1, 0.84)	0.86 (0.24, 3.16)	0.825
Shock	3.029 (1.821, 5.04)	0.48 (0.20, 1.15)	0.101
Respiratory Failure	3.67 (2.30, 5.86)	4.84 (2.47, 9.48)	<0.001
Acute Liver Failure	3.23 (1.15, 9.09)	0.68 (0.17, 2.75)	0.585
Hypoglycemia	3.33 (1.92, 5.78)	2.98 (1.34, 6.62)	0.007
Glycemic variability	1.02 (1.00, 1.04)	1.00 (0.98, 1.03)	0.798
Use of insulin	0.54 (0.29, 0.98)	0.19 (0.08, 0.48)	<0.001
Use of glucocorticoids	2.65 (1.60, 4.39)	1.19 (0.58, 2.42)	0.642
Use of vasopressors	10.02 (6.12, 16.40)	13.67 (6.39, 29.23)	<0.001

Only variables with p value <0.2 in the bivariable regression are depicted here; 1: Reference category.

3.5. Length of Stay and Duration of Mechanical Ventilation

A Mann-Whitney U test was performed to evaluate whether Length of stay and duration of MV differed by hyperglycemia, hypoglycemia and high GV. The results indicated that patients with hyperglycemia and hypoglycemia had significantly longer LOS than patients without hyperglycemia and hypoglycemia respectively, ($z = -4.83$, $p = < 0.001$ & $z = -2.83$,

$p = 0.005$ respectively). There was no significant difference between the LOS of patients with high GV and normal GV, ($z = -0.64$, $p = 0.53$). Similarly, patients with hyperglycemia and hypoglycemia also had significantly longer duration of MV than patients without hyperglycemia and hypoglycemia respectively, ($z = -2.07$, $p = 0.04$ & $z = -4.46$, $p = < 0.001$ respectively). And there was no significant difference between the duration of MV of patients with high GV and normal GV, ($z = -0.53$, $p = 0.60$).

Table 5. Glycemic profiles and Length of stay in the ICU.

Glycemic profiles		Count	Length of stay (Days)			p value
			Mean	Median	IQR	
Hyperglycemia	No	38	3.32	2	1-4	<0.001
	Yes	354	8.15	6	3-9	
Hypoglycemia	No	328	7.05	5	3-8	0.005
	Yes	64	10.91	6.5	3.5-13.5	
High GV	No	316	7.91	5	3-9	0.53
	Yes	76	6.74	4.5	3-8	

Table 6. Glycemic profiles and duration of MV.

Glycemic profiles		Count	Duration of MV (Days)			p value
			Mean	Median	IQR	
Hyperglycemia	No	38	1.11	0	0-2	0.04
	Yes	354	3.44	1	0-5	
Hypoglycemia	No	328	2.49	0	0-3	<0.001
	Yes	64	6.88	3	0-7	
High GV	No	316	3.27	1	0-4	0.60
	Yes	76	2.97	1.5	0-4	

4. Discussion

Our study aimed to determine the effect of multiple glycemic parameters on ICU mortality and clinical outcomes in critically ill patients. The prevalence of hyperglycemia in the sample was 90.3% which is in line with the prevalence of 40-90% which is reported worldwide by different studies, and higher than the studies done in Egypt [2, 20, 21]. It is worth noting that there are significant inconsistencies between the cutoff blood glucose used by the different studies mentioned in this paper. The prevalence of hypoglycemia was 16.3% which is higher than the 5% prevalence reported in the retrospective analysis of 52,107 ICU patients done in Hong Kong and lower than the 37% prevalence reported from a multicentric study from Netherlands and USA [22-24]. The prevalence of high glucose variability was estimated to be 19.4%.

From the markers of dysglycemia, hyperglycemia, hypoglycemia and high glycemic variability, only hypoglycemia has a significant independent association with mortality. This finding was also demonstrated in an observational study done in Australia which showed higher mortality of hypo-

glycemia as compared to normoglycemia [25]. Patients with hypoglycemia also had significantly longer LOS and longer duration of MV. An increased length of stay was also associated with hypoglycemia in a review of 6240 critically ill patients, and the more the number of hypoglycemic events, the longer the length of stay. Independent of the severity of the disease, even a single episode of hypoglycemia (70 mg/dL) led to a significantly longer length of stay [18, 23]. This association was also reflected in our study. In contrast to our findings of longer MV duration in hypoglycemic patients, a recent study done in Brazil in 542 ICU patients found out hypoglycemia was independently associated with increased mortality and increased need of MV but shorter duration of ICU and hospital length of stay, and shorter duration of MV [26]. But this Brazilian study of assessed hypoglycemia within the first 24 hours of ICU admission, and the association with shorter duration of stay was controlling disease severity for SAPS 3 (Simplified Acute Physiology III) score, which was one of the main limitations of our study.

Our study did not show that hyperglycemia had a significant association with mortality, but it did show patients with hyperglycemia had increased LOS and duration of mechani-

cal ventilation. The association between hyperglycemia and mortality varied in different literatures. A retrospective cohort study including 259,040 ICU admissions found that increasing severity of hyperglycemia was associated with increased mortality. However, a more recent meta-analysis which included 18,098 patients from 35 studies across the spectrum of adult critical care did not find significant differences in hospital mortality between four glycemic control categories (<110 mg/dl, 110-144 mg/dl, 144-180 mg/dl and >180 mg/dL) [27]. The Brazilian study mentioned above also found that one of the poor outcomes associated with stress hyperglycemia, especially within the first 24hrs after ICU admission was increased need for MV similar to our finding of significantly longer duration of mechanical ventilation in patients with hyperglycemia [26].

High GV in contrast did not have a significant effect on mortality, LOS and duration of MV. A Prospective Observational Study done in India found there was a significant in hospital and ICU mortality which is associated with increasing levels of GV, measured by CV, which our study did not reproduce. Although they used different measurements for GV, the study done in Brazil showed a statistically significant association between high GV between mortality, ICU LOS and duration of mechanical ventilation [26].

Our logistic regression analysis also revealed a statistically significant association between insulin use and mortality. Patients who used insulin had a lower likelihood of mortality compared to those who did not use insulin. There was a significant positive relationship between hyperglycemia and dose of insulin indicating higher frequency hyperglycemia was associated with the requirement of higher doses of insulin. There was a significant positive relationship between BG between 140-180 mg/dL and dose of insulin but there was no statistically significant relationship between hypoglycemia and dose of insulin. This suggests patients who were being treated with insulin were not developing hypoglycemia and were achieving within target BG. So, in our study the benefit that patients on insulin therapy drew regarding the mortality benefit is potentially from the achieving within target BG.

The positive relationships between hyperglycemia, the dose of insulin and frequency of within target blood glucose levels underscore the need for vigilant glycemic management to achieve target glucose levels. These findings contribute to the existing literature on emphasizing the potential benefits of insulin therapy in critically ill patients targeting blood glucose levels between 140-180 mg/dL, while avoiding hypoglycemia. This is in keeping with the finding of the NICE-SUGAR trial and recommendations of the American diabetic association [28, 29].

The other key finding of our study is age-combined CCI, respiratory failure, use of vasopressors and hypoglycemia, as mentioned above, were independent predictors of mortality. The absence of established scoring systems for severity of illness like APACHE, SOFA, or SAPS3 may limit the ability to fully understand the impact of illness severity on mortality

outcomes in our study population. The predictors identified in our study could be confounded by the severity of illness. However, a study done at Hawassa University Comprehensive Specialized Hospital demonstrated that the mere requirement of mechanical ventilation and presence of shock during admission were independent predictors of ICU mortality [1].

5. Conclusion

Dysglycemia, i.e. hypoglycemia, hyperglycemia, and high glycemic variability, is very prevalent among patients admitted in the ICU and it is potentially associated with adverse outcomes. Hypoglycemia was associated with significantly longer ICU LOS, longer duration of MV, and higher mortality. Similarly, hyperglycemia was associated with longer ICU LOS and longer duration of MV, but not with higher mortality. There was no strong impact of high glycemic variability on ICU LOS, duration of MV, or mortality. Achieving target blood glucose levels of 140–180 mg/dL in critically ill patients may be advantageous, as suggested by the association between the use of insulin and lower mortality rates. Further research to explore the impact of glycemic control on clinical outcomes in patients admitted to the ICU considering and incorporating severity of illness scores is required.

Abbreviations

ADA	American Diabetic Association
AOR	Adjusted Odds Ratio
APACHE	Acute Physiology and Chronic Health Evaluation
BG	Blood Glucose
CCI	Charlson Comorbidity Index
CRP	C-reactive Protein
CV	coefficient of Variance
DM	Diabetes Mellitus
GV	Glycemic Variability
HbA1c	Glycohemoglobin, Hemoglobin A1c
HMIS	Health Management Information System
ICU	Intensive Care Unit
IQR	Interquartile Range
LOS	Length of Stay
MV	Mechanical Ventilator
OR	Odds Ratio
SD	Standard Deviation
SAPS3	Simplified Acute Physiology III
SOFA	Sequential Organ Failure Assessment
SPHMMC	St. Paul's Hospital Millennium Medical College
TASH	Tikur Anbessa Specialized Hospital
VTE	Venous Thromboembolism

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Author Contributions

Wasihun Zerfu Zewde: Conceptualization, Methodology, Formal analysis, Writing—original draft. Writing—review and editing, Project administration

Amare Gulilat Mamo: Supervision, Validation, Methodology

Helina Yohannes Afework: Data curation, Investigation

Mahlet Mitiku Desalegn: Software, Resources

Ermias Berehanu Hayle: Visualization, Methodology

Zewdu Abadi Tsegay: Writing – review & editing

Mehariw Wondim Netsere: Writing – review & editing, Resources

Amir Muhidin Abraham: Softwares, Data curation

Yeabtsega Amlaku Asres: Data curation, Investigation

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Data Availability Statement

The data is available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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Biography



Wasihun Zerfu Zewde is a 2024 graduate of internal medicine from SPHMMC currently working in Arbaminch General Hospital. He completed his undergraduate studies from Addis Ababa University in 2018. He has worked in the rural parts of Ethiopia for 2 years before joining residency program.