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Original Research Article

Incidence, Predictors, and Outcome of Stress Hyperglycemia in Critically Ill Adult Patients Admitted in Medical and Surgical Intensive Care Units at Muhimbili National Hospital Tanzania

Alice D. Gwambegu[1*], Tumaini Nagu[1, 2, 3], Grace Shayo[1, 2, 3]

[1]Hubert Kairuki Memorial University, Department of Internal Medicine, Dar es salaam, Tanzania
[2]Muhimbili National Hospital, Department of Internal Medicine, Mloganzila Dar es salaam, Tanzania
[3]Muhimbili National Hospital, Department of Internal Medicine, Upanga Dar es salaam, Tanzania

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Abstract: ***Background:*** Stress hyperglycemia is common among critically ill patients admitted in the intensive care units (ICU), affecting 17-68%of patients within the first 48 hours of admission. Long-term stress hyperglycemia is linked to poor clinical outcomes and increases mortality. The burden and outcomes of stress hyperglycemia in critically ill patients is unknown in Tanzania. ***Methodology:*** Prospective short-term cohort study was conducted at Muhimbili National Hospital for 6 months. Adult critically ill patients in medical and surgical ICU were recruited consecutively. On admission, HbA1c and RBG were checked. FBG/RBG was tested daily until discharge or death. Stress hyperglycemia was defined as FBG≥6.1mmol/l or RBG of 140mg/dl (7.8mmol/L) or more observed during ICU admission. Length of stay and ICU mortality in one month of follow-up were recorded. SH proportion is reported as percentages. Predictors of SH were analyzed using logistic regression. P value <0.05 was considered statistically significant. Kaplan Meier's mortality curves were used to compare the mortality of patients with SH to those without. ***Results:*** A total of 270 patients were enrolled, among them 120/270(44.4%) developed SH. These patients were largely male (58.2%) with a mean age of 48.2±17.8years. predictors of SH were having comorbidities and the use of steroids. Stress hyperglycemia increased the risk of staying in the ICU for ≤ 5 days by 2 folds aOR (95%CI), 2.416 (1.261-4.629) P=0.008. Steroid use reduces the risk of SH by 67% aOR (95%CI), 0.326 (0.167-0.636) P=0.001 and by 78% for patients with other comorbidities aOR (95%CI), 0.2196(0.097-0.497) P<0.001. ***Conclusion:*** The incidence of stress hyperglycemia is high in ICU patients as evidenced in this study. Duration of ICU stay, comorbidities, and steroid use was significantly associated with stress hyperglycemia. Stress hyperglycemia contributes to a higher mortality rate among critically ill patients.

Keywords: Stress hyperglycemia, critically ill patient, ICU.

INTRODUCTION

The burden of stress hyperglycemia

Hyperglycemia complicates the course of illness of many critically ill patients contributing to increased morbidity and mortality in adult intensive care units (ICUs) [1–5]. Previous studies report the prevalence of stress hyperglycemia on admission to range from 17% to 68%. The Incidence density of stress hyperglycemia among patients without previous diabetes, whose glucose levels were measured during admission is reported to be 15.72 people per 1000 patients hospitalized with about 12% cumulative incidence of SH [6]. In another study by Amina Godinjak1 *et al*., it was found that out of 100 critically ill patients admitted to the ICU, 19% of them developed stress-hyperglycemia (glucose> 11.1 mmol / l) with 17.4 ± 9.6 mmol/l being the mean value of blood glucose recorded [7]. An observational study by L. S. Williams et al described the prevalence of hyperglycemia to be ranging from 32% to 38% in community hospitals [3,4]. In Tanzania critical illness Stress hyperglycemia had previously been investigated among patients with tuberculosis and revealed a prevalence of 17.1 % [8].

***Corresponding Author:** Alice D. Gwambegu
Hubert Kairuki Memorial University, Department of Internal Medicine, Dar es salaam, Tanzania

Risk factors for stress hyperglycemia

In the same study by Amina Godinjak1 *et al*., the recorded reasons for admission to the ICU were grouped into respiratory, cardiovascular, sepsis / septic shock, neurologic, and others of which 43 %, 17 %, 15 %, 15 %, and 10 % respectively developed hyperglycemia while in the ICU [9]. Stress hyperglycemia is also frequently reported in critically ill patients suffering from Traumatic Brain Injury and subarachnoid hemorrhage (SAH), tuberculosis, stroke, and acute coronary syndrome as well as patients who undergo cardiac surgery [2,9–11]. Among these risk factors patients with stress hyperglycemia following traumatic brain injury (TBI) and subarachnoid hemorrhage (SAH) are reported to be associated with a high mortality rate compared to the rest [12].

However several drugs are reported to induce hyperglycemia when used in higher doses and for a long time through various mechanisms. Including insulin resistance, an increase in hepatic glucose production, decreasing insulin secretion, glucose intolerance, and autoimmune destruction of beta cells, among others. Steroids being the main cause of drug-induced hyperglycemia do increase insulin resistance by up to 46% and lead to an increase of the baseline glucose by up to 68% [13]. Beta-blockers hinder insulin release by blocking pancreatic beta receptors [14] Statins bring about cholesterol-dependent conformational changes in glucose transporters (GLUTs) which hampers glucose uptake resulting in hyperglycemia [14] while diuretics cause depletion of serum potassium resulting in impaired insulin release [15].

Impacts of stress hyperglycemia on critically ill patients

The duration of stay in the intensive care unit was found to be higher in patients with stress hyperglycemia ranging between 3-78 days than in those without ranging between 3–31 days while the duration of stay in hospital was found to be higher in patients with stress hyperglycemia ranging from 3-101 days than in those without ranging from 3-50 days [16]. Stress hyperglycemia has been reported as a public problem in critically ill patients, regardless of the acute condition they are exposed to, and is also reported to be associated with bad outcomes in the intensive care unit [16].

Many studies have also reported the presence of stress hyperglycemia to be associated with an increased risk of mortality in critically ill patients than those who do not develop stress hyperglycemia [6,17,18]. A study conducted in Kayseri, Turkey reported a mortality rate in the intensive care unit to be 20% of all admissions. Twenty-eight percent of these deaths occurred among those with stress hyperglycemia while the rate was 5.6% in those without stress Hyperglycemia [16]. In a meta-analysis of 26 cohort studies on mortality and/or functional recovery after stroke in relation to admission glucose level done by comparing relative risks in hyperglycemia and normoglycemic patients with or without diabetes, it was reported that following ischemic stroke, admission glucose level >6.1 to 7.0 mmol/L (110 to 126 mg/dL) was associated with 3 times increased risk of in-hospital or 30-day mortality in non-diabetic patients only with a relative risk of 3.28 to 4.64 (95% CI, 2.32) and after a hemorrhagic stroke, nondiabetic stroke survivors whose admission glucose level were >6.7 to 8 mmol/L (121 to 144 mg/dL) were found to have a greater risk of poor functional recovery with a pooled unadjusted relative risk of poor functional recovery of 51.41; 95% CI, 1.16 to 1.73 [19].

It was then concluded that acute hyperglycemia predicts an increased risk of in-hospital mortality after ischemic stroke in non-diabetic patients and an increased risk of poor functional recovery in non-diabetic stroke survivors [20]. The reported length of hospital stay (LOS) among critically ill patients requiring ICU was an IQR of 3–10 days with a median LOS of 5.5(±SD??) days. Another study by Suleiman et al investigated the prevalence of hyperglycemia and its role as a predictor of mortality in acutely ill older patients admitted to a high-dependency care unit in Italy. This study found that out of 822 patients without known diabetes, 104 (12.7%) had hyperglycemia on admission [21]. It also demonstrated that newly recognized hyperglycemia (≥10.0 mmol/l) was independently associated with mortality with an adjusted OR of 2.7 (95% CI 1.6 to 4.8) [21].

MATERIALS AND METHODS

Study type and design

This study was a prospective short-term cohort study where patients were followed from the date of admission to the ICU until death or 30 days in the ICU or in their surgical and medical ward. We obtained mobile phone numbers of both patients and next of kin to assist in the follow-up of patients that would have been discharged home before 30 days however none of our study patients was discharged home before 30 days.

Study population

The target population was critically ill patients admitted to the medical and surgical ICU at MNH.

Inclusion criteria

- Age 18 years or older.
- Patients whose relatives gave consent and agreed to sign a written consent form on patients' behalf if the patient could not do it due to illness.

Exclusion criteria

- Those with glycemic-related causes as the primary reason for admissions to ICU such as diabetes ketoacidosis, hyperosmolar hyperglycemia syndrome, or hypoglycemia.

- Blood transfusion at admission or within 24 hours of admission to ICU as this may give false positive HBA1c results.

Sample size

Upon retrospective review of the recorded data of critically ill patients in the ICU admission books in the medical and surgical ICU, it was found that an average of 3 patients was admitted in 2 days. Based on the theoretical assumptions that critically ill patients admitted to the ICU develop stress hyperglycemia with a total of 270 patients recruited the power of 80% was met by this study.

Enrollment of study participants

Consecutive recruitment of participants was done. From the critically ill patients admitted in the medical and surgical ICU, blood glucose levels were obtained at admission by using a *gluco-plus* glucometer as well as measurements of glycated hemoglobin (HbA1c) to capture those with undiagnosed type 2 diabetes mellitus (T2DM). A blood sample for glycated hemoglobin was sent to the MNH central laboratory for testing. Follow-up RBG was measured daily in the following days post admission in the ICU to assess whether they developed hyperglycemia during their critically ill state in the ICU. Patients whose fasting blood glucose levels were ≥6.1mmol/l or RBG of 140mg/dl (7.8mmol/L) or more and HbA1c of <6.5% were considered to have stress hyperglycemia. Those with HbA1c ≥6.5% who had not been diagnosed to have DM before were regarded as newly diagnosed diabetic patients [22]. DM was diagnosed if the patient had a pre-existing diagnosis of DM or was taking anti-diabetics drugs before the critical illness and both those with a known diagnosis of Diabetes mellitus together with those who are newly diagnosed DM patients were excluded from the study. Those with FBG <6.1mmol/l or RBG of <11.1 mmol/l were considered to have no diabetes.

Eligible participants were categorized into those with the stress hyperglycemia group and those without the stress hyperglycemia group. In the two groups, the cause for ICU admission and history of Diabetes in the family was obtained from the file, and the outcome of interest which includes the duration of stay in the ICU and the rate of mortality within one month after discharge from ICU to medical and surgical ward were explored.

Methods and data collection tools

A clinical data extraction form was used to collect information about the patient's demographic and clinical characteristics (disease history and physical examination) details from the patient's files. However, a checklist and data sheet was used to crosscheck the accuracy and completeness of intended data and record patients' measurements respectively. About 5mls of venous whole blood sample was collected once from one of the patient's hands and sent to the central laboratory where glycated hemoglobin levels were tested using Abbot Architec i1000SR machine and a pinprick to obtain a drop of capillary blood for random blood glucose test. Fasting and random blood glucose (FBG and RBG) testing was measured daily using "STANDARD^{TM} GlucoNavii GDH blood Glucose Meter issued in 2020 made in Korea" for follow-up of those who were initially not hyperglycemic after initial testing. Patients were followed up to 30 days after ICU admission or until death. Those who were discharged to the general medical or surgical ward were followed up to 30 days; patients' and next of kin's phone numbers were recorded for further follow-up of those who would be discharged before the end of 30 days, however, none of our patients was discharged home before 30days.

Data processing and analysis

Data was entered and analyzed using SPSS version 23. Incidence cases of stress hyperglycemia were summarized as proportions whereby the number of patients developing SH was divided by the total number of the studied population. Logistic regression was performed to detect the independent predictors of stress hyperglycemia where variables with a p-value <0.2 in univariate analysis were entered into the multivariate analysis model. In the multivariate model, a p-value <0.05 was considered to be statistically significant. Kaplan Meier mortality curve was used to compare the cumulative proportion of mortality of patients with stress hyperglycemia and those without stress hyperglycemia within 30 days of follow-up.

RESULTS

Socio-demographic and clinical characteristics of patients

Figure 3 summarizes the flow of the patients where in a period of 6 months of the study, from September 2021 to February 2022, a total of 701 critically ill patients were admitted to the medical and surgical ICU. Out of 701 patients, 564 patients were approached of which 179 were admitted due to DM and DM complications, 92 had high levels of HBA_1C at baseline and 23 patients were aged <18yrs.

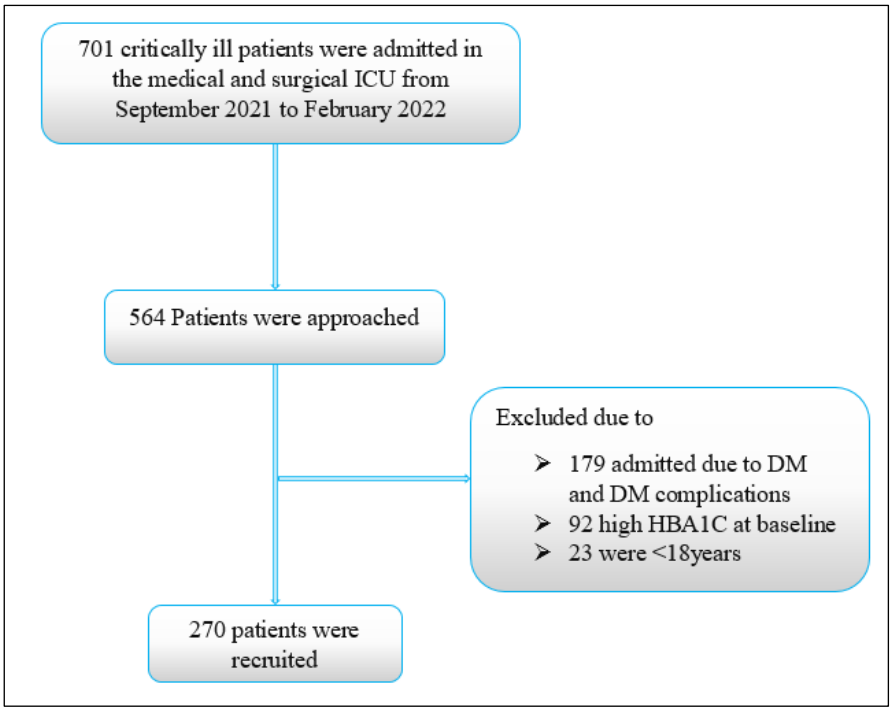

Figure 1: Flow diagram showing the recruitment process of patients

Out of 270 patients who were recruited, 58.2% of patients were males and 41.8% were female. The mean age was 48.22 ± D17.8 where 128 (47.41%) were younger than 45 years while 73(27.03%) were more than 60 years old. A total of 98(36.30%) had a family history of DM while 100 (37.03%) had an unknown family history of DM. Out of all patients 137 (50.74%) patients were using medications such as steroids 93 (34.44%), statin 52(19.26%), beta-blockers 40(14.817%), and 14(5.56%) were using thiazides. A total of 127(47.04%) patients had comorbidities where 11.5% were hypertensive, 11.1% had CKD, and 7.4% had HIV. Those with HBA_1C within a normal range were more than half 152 (56.30%) and 118(43.7%) had a pre-diabetic level (5.7% - 6.4%). Out of all patients 146 (54.07%) patients stayed in the ICU for ≤ 5 days while 124 (45.93%) stayed for >5 days. The reasons for ICU admission were grouped into respiratory 30(11.11%), sepsis 20 (7.41%), neurology 68(25.19%), nephrology 16(5.93%), surgical 115(42.59%) and 21(7.77%) others (OBGYN, cardiovascular and HIV associated illness) (Table 1).

Table 1: Socio-demographic and clinical characteristics of patients of stress hyperglycemia of critically ill patients admitted to the medical and surgical ICU at MNH. N=270

	Frequency	Percentage
Age (Mean 48.22 ± SD 17.08)		
<45	128	47.41
45 – 60	69	25.56
>60	73	27.03
Sex		
Male	157	58.15
Female	113	41.85
BMI from estimated body weight		
Underweight	10	3.70
Healthy weight	138	51.11
Overweight	90	33.33
Obese	32	11.85
Family history of DM		
Yes	98	36.30
No	72	26.67
Unknown	100	37.03
Medications		
Steroids		
Yes	93	34.44

No	177	65.56
Statins		
Yes	52	19.26
No	218	80.74
Beta blockers		
Yes	40	14.81
No	230	85.19
Thiazides		
Yes	14	5.56
No	256	94.44
Presence of Comorbidities		
Yes	120	44.44
No	150	55.56
HIV*		
Yes	20	7.41
No	250	92.59
Hypertension*		
Yes	105	38.89
No	165	61.11
CKD*		
Yes	30	11.11
No	240	88.89
Heart disease*		
Yes	31	11.48
No	239	88.52
HBA_1C levels		
4% - 5.6%	152	56.30
5.7% - 6.4%	118	43.70
Duration of ICU stay		
≤ 5 days	146	(54.1)
>5 days	124	(44.9)
Reason for ICU admission		
Respiratory	30	11.11
Sepsis	20	7.41
Surgical	115	42.59
Nephrology	16	5.93
Neurology	68	25.19
Others	21	7.77

NB: *The sum of patients with comorbidities (186) exceeds the number of patients with comorbidities (120) because some patients presented with more than 1 comorbidity hence counted more than once.

Incidence of stress hyperglycemia among critically ill patients admitted in the medical and surgical ICU at MNH. N=270.

This study found that a total of 120/270 (44.4%) developed stress hyperglycemia during ICU admission. More than half of these 78/120(65%) developed stress hyperglycemia within the first 48 hours of ICU while 42/120 (35.0%) developed stress hyperglycemia after 48 hours of ICU admission (Table 2).

Table 2: Incidence of stress hyperglycemia among critically ill patients admitted to the medical and surgical ICU at MNH. N=270

Variable	Frequency	Percentage
Total patients with stress hyperglycemia	120	120/270 (44.4%)
Patents without stress hyperglycemia	150	150/270 (55.6%)

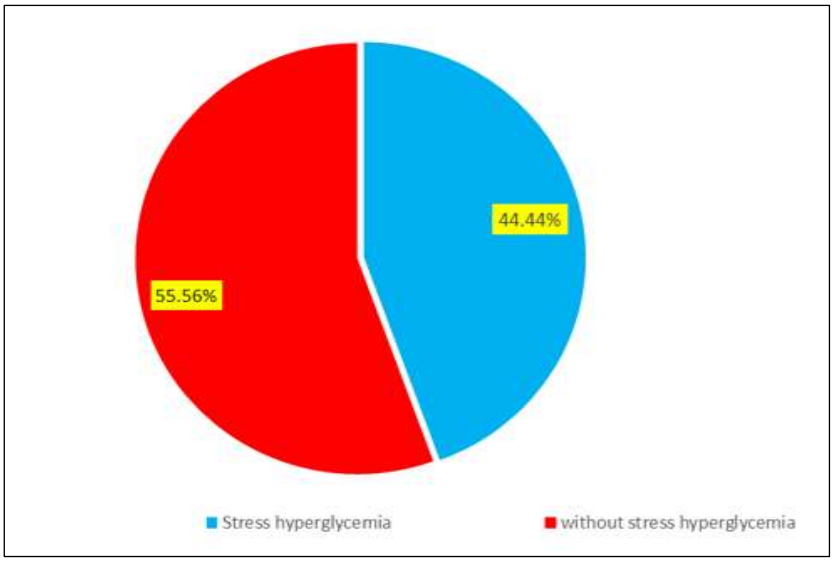

Figure 2: Incidence of stress hyperglycemia among critically ill patients admitted to the medical and surgical ICU at MNH

Factors associated with stress hyperglycemia of critically ill patients admitted in the medical and surgical ICU at MNH. N=270.

This study found no significant association between age and the development of stress hyperglycemia during the first 48 hours of ICU admission with P values of 0.640 however there was a significant association between the development of stress hyperglycemia and age with a P value of 0.037 after 48hours where a majority of those who developed stress hyperglycemia after 48hours were aged between 45 and 60 years (n=16(23.19%)).

Patients with a pre-diabetic range of HBA1C (5.7%-6.4%) were more likely to develop stress hyperglycemia within 48hours and after 48hours of their ICU admission n=51(64.56%) P=0.001 and n=28(23.73%) P=0.001 respectively during their ICU admission than those with normal ranges. Individuals with a family history of diabetes were more likely to develop stress hyperglycemia than those without and with an unknown family history of diabetes 42 (53.16%) versus n=19 (24.05%) and n=18 (22.79%) respectively P=<0.001 as well as stress hyperglycemia n=18(25.00%) versus n=13(13.26%) without family history and n=10(9.80%) respectively P=0.018.

Moreover, patients using steroids n=43(54.43%) P=<0.001 and n=21(15.22%) P=0.015 developed stress hyperglycemia within 48 hours and stress hyperglycemia after 48 hours respectively compared to those not using the steroids. The use of beta blockers n=11(13.92%) p=0.752, statins n=16(20.25%) P=0.01 and thiazides n=3(20.00%) P=0.583 was not associated with development of stress hyperglycemia. Patients who stayed in the ICU for >5 days developed stress hyperglycemia more n=83(76.9%) than those who stayed for ≤ 5 days n=53(32.7%) respectively however the difference in duration of ICU stay was not statistically significant P=0.160 (Table 3).

Table 3: Factors associated with stress hyperglycemia among critically ill patients admitted to the medical and surgical ICU at MNH. N=270

Stress Hyperglycemia Within 48hours			**Stress Hyperglycemia After 48hours**	
Variable	**Frequency**	**P Value**	**Frequency**	**P Value**
Age				
<45	35 (44.31%)		13(10.00%)	
45 – 60	23 (29.11%)	0.640	16(23.19%)	0.037
>60	21 (26.58%)		12(16.44%)	
Sex				
Male	42 (53.16%)		26(16.56%)	
Female	37 (46.84%)	0.321	15(13.16%)	0.453
BMI from estimated body weight				
Underweight	3 (3.80%)		2(20.00%)	
Healthy weight	38 (48.10%)		14(10.00%)	
Overweight	29 (36.71%)	0.924	14(15.56%)	0.007

Obese	9 (11.39%)		11(34.38%)	
Family history of DM				
No	19 (24.05%)		13(13.26%)	
Yes	42 (53.16%)	<0.001	18(25.00%)	
Unknown	18 (22.79%)		10(9.80%)	0.018
HBA1c Levels				
4% - 5.6%	28 (35.44%)		13(8.44%)	
5.7% - 6.4%	51 (64.56%)	<0.001	28(23.73%)	<0.001
Medications				
Steroids				
Yes	43 (54.43%)		21(15.22%)	
No	36 (45.57%)	<0.001	20(14.93%)	0.015
Statins				
Yes	16 (20.25%)		14(26.14%)	
No	63 (79.75%)	0.816	27(12.33%)	0.010
Beta-blockers				
Yes	11 (13.92%)		10(24.39%)	
No	68 (86.08%)	0.752	31(13.42%)	0.070
Thiazides				
Yes	6 (7.59%)		3(20.00%)	
No	73 (92.41%)	0.329	38(14.79%)	0.583
Comorbidities				
Yes	53 (67.09%)		28(21.88%)	
No	26 (32.91%)	<0.001	13(9.03%)	0.003
Condition of ICU Admission				
Respiratory	13(16.46%)		8(25.81%)	
Infection	7 (8.86%)		3(15.00%)	
Surgical	28 (35.44%)		14(12.17%)	
Nephrology	4 (5.06%)		2(12.50%)	
Neurology	18 (22.78%)		13(18.84%)	
Other	9 (11.39%)	0.403	1(4.76%)	0.293
Time of ICU stay				
≤ 5 days	53(67.95%)			
>5 days	25(32.1%)	0.160	28(66.67%)	<0.001

Predictors of stress hyperglycemia among critically ill patients admitted in the medical and surgical ICU at MNH. N=270

During univariate analysis to identify the predictors of stress hyperglycemia, patients aged between 45-60years were less likely to develop stress hyperglycemia by 25 % cOR (95%CI) 0.753(0.399-1.419) P= 0.380 compared to the other age groups. Compared to female patients, males had a 31% high risk of developing stress hyperglycemia cOR (95%CI), 1.308(0.769-2.225) P= 0.3211. Compared to those who stayed ≤5 days in the ICU, patients who stayed for >5 days had a 61% increased risk of developing stress hyperglycemia cOR (95%CI), 1.614(0.927-2.811) P=0.091. Patients who were using steroids among their medications had a 68% low risk of developing stress hyperglycemia compared to those who were not using steroids cOR (95%CI), 0.318(0.184-0.550) P=0.000. Patients with CKD had 73% more risk of developing stress hyperglycemia compared to those with other comorbidity cOR (95%CI), 1.732(1.016-2.953) P=0.044 (Table 4).

In a multivariate analysis, predictors of developing stress hyperglycemia among patients admitted to medical and surgical ICU were duration of ICU stay and comorbidities. Stress hyperglycemia increased the risk of staying in the ICU for ≤ 5 days by 2 folds, aOR (95%CI), 2.416(1.2614.629) P= 0.008. Patients who were using steroids among their medications had a 67% reduced risk of developing stress hyperglycemia within the first 48hours of ICU admission but not after 48hours than those who were not using aOR (95%CI), 0.326(0.167-0.636) P=0.001. Patients with comorbidities had a 78% reduced risk of developing stress hyperglycemia than those without aOR (95%CI), 0.219(0.097-0.497) p<0.00 (Table 4).

Table 4: Logistic analysis of predictors of stress hyperglycemia among critically ill patients admitted to the medical and surgical ICU at MNH. N=270

Univariate analysis					Multivariate analysis	
Variables		**N (%)**	**Crude OR(95%CI)**	**P Value**	**Adjusted OR(95%CI)**	**P Value**
Age	≤ 45	35(27.3%)	Ref	Ref		
	45-60	23(33.3%)	0.753(0.399-1.419)	0.380		
	> 60	20(27.4%)	0.997(0.523-1.900)	0.993		
Gender	Male	42(26.6%)	1.308(0.769-2.225)	0.321		
	Female	36(32.1%)	Ref			
Steroids use	Yes	42(44.7%)	0.318(0.184-0.550)	0.000	**0.326(0.167-0.636)**	**0.001**
	No	36(20.5%)	Ref		Ref	
Thiazides use	Yes	6(40%)	0.590(.203-1.718)	0.333		
	No	72((28.2%)	Ref			
Beta blockers	Yes	11(26.8%)	0.887(0.420-1.872)	0.752		
	No	67(29.3%)	Ref			
Statins	Yes	16(30.2%)	0.925(0.48-1.783)	0.816		
	No	62(28.6%)	Ref			
Time ICU stay	>5 days	25(32.1%)	Ref		Ref	
	≤ 5 days	53(67.9%)	1.614(0.927-2.811)	0.091	**2.416(1.261-4.629)**	**0.008**
Comorbid conditions	Yes	52(40.6%)	0.328(0.189-0.569)	0.000	**0.219(0.097-0.497)**	**<0.001**
	No	26(18.3%)	Ref		Ref	
HIV	Yes	9(45.0%)	0.466(0.185-1.173)	0.105	1.699(0.52-5.55)	0.380
	No	69(27.6%)	Ref		Ref	
CKD	Yes	38(35.8%)	1.732(1.016-2.953)	0.044	1.699(0.52-5.55)	0.380
	No	40(24.2%)	Ref		Ref	
Heart disease	Yes	8(25.8%)	1.191(0.508-2.790)	0.688		
	No	70(29.3%)	Ref			
Hba1c levels	4.0-5.6%	4(21.1%)	Ref			
	5.7-6.49%	74(29.5%)	0.638(0.205-1.986)	0.438		
Disease conditions	Respiratory	13(41.9%)	0.852(0.274-2.647)	0.782	1.427(0.349-5.839)	0.621
	Infections	7(35.0%)	1.143(0.32-4.081)	0.837	1.419(0.303-6.644)	0.657
	Surgical	28(24.8%)	1.868(0.702-4.972)	0.211	1.202(0.363-3.984)	0.763
	Nephrology	4(25.0%)	1.846(0.440-7.745)	0.402	2.417(0.364-16.033)	0.361
	Neurology	18(26.1%)	1.744(0.621-4.892)	0.291	3.35(0.863-13.008)	0.081
	Others	8(38.1%)	Ref		Ref	

Thirty (30) day mortality among critically ill patients with stress hyperglycemia and those without stress hyperglycemia.

In our study, the ICU mortality rate was found to be 156/270 (58%). Mortality in patient group with stress hyperglycemia 82/156(53%) was determined higher compared to 74/156 (47%) of those without stress hyperglycemia, P value= 0.031 (Table 5). In the survival analysis using Kaplan Meier mortality curve**,** the cumulative mortality rate of patients was found to be higher among those who developed stress hyperglycemia within 48hours, followed by those with stress hyperglycemia after 48hours compared to those who did not develop stress hyperglycemia. These differences were statistically significant with a Log Rank (Mantel-cox) of <0.001. Figure 3 and when comparing mortality between those with and without stress hyperglycemia patients with stress hyperglycemia were found to have a higher cumulative mortality rate than those without however these differences were only numerical difference but not statistically significant with Log Rank (Mantel-cox) of 0.499 (Figure 3).

Table 5: Rate of mortality among critically ill patients with stress hyperglycemia admitted in the medical and surgical ICU at MNH. N=120

Category	Total (N)	Death	P-Value
With stress hyperglycemia	120	82/156(53%)	0.031
Without stress hyperglycemia	150	74/156(47%)	
Total	270	156/270(58%)	

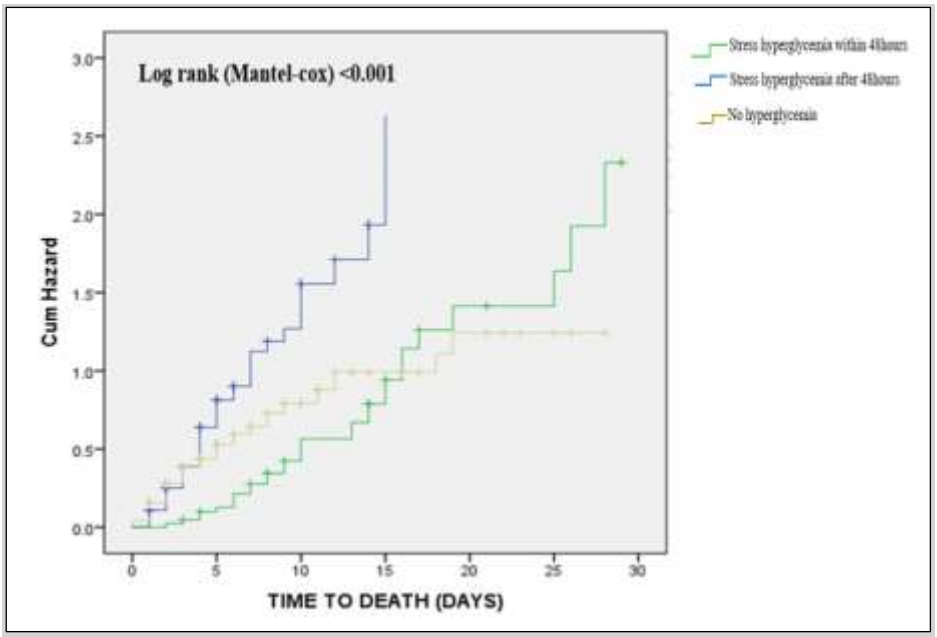

Figure 3: Kaplan Meier mortality curves comparing the mortality of critically ill patients with stress hyperglycemia (SH) within 48hours, stress hyperglycemia after 48hours and mortality of critically ill patients without stress hyperglycemia (No HG)

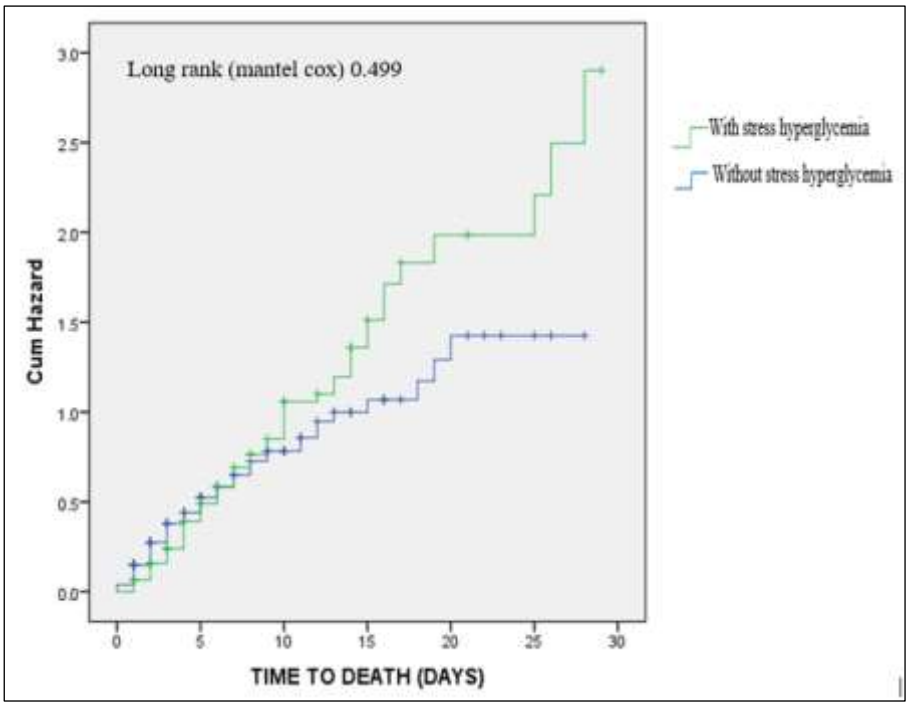

Figure 4: Kaplan Meier mortality curves comparing the mortality of critically ill patients with stress hyperglycemia and those without stress hyperglycemia

DISCUSSION

This study aimed to determine the incidence, predictors, and outcomes of stress hyperglycemia in critically ill patients who had normal blood levels of glucose during admission to the ICU but later developed stress hyperglycemia and assessed the effects of stress hyperglycemia on morbidity and mortality to critical ill patients as compared to those who did not develop stress hyperglycemia while in the ICU. The overall incidence of hyperglycemia was found to be 44.4%, of which 29.3% of the patients developed stress hyperglycemia within 48 hours of ICU admission. This is the first study in our country to study stress hyperglycemia among critically ill patients in the ICU, however, the overall incidence of stress hyperglycemia in the present study is comparable to the findings from a study by Umpierrez et al, 2002 that reported 28.2% of stress hyperglycemia with 38% of overall incidence of hyperglycemia [23] and study by Russo et al, done in Italy in 2017 that reported an overall prevalence of

hyperglycemia to be 40.40% [6]. In a study reported by Sharma, *et al.,* (2017) among medical ICU patients in India the incidence of stress hyperglycemia was slightly lower than what is reported in the present study because Sharma *et al.,* studied critically ill patients who were not very sick, with fewer physical stress and therefore more likely to have lower glycemic levels than the very sick patients [24].

This study found that the duration of ICU stays, comorbidities, and the use of steroids were associated with the development of stress hyperglycemia. These findings were similar to those reported by other Temel *et al.,* which reported a longer duration of stay in the intensive care unit in patients with stress hyperglycemia ranging between 3-78 days than in those without ranging between 3– 31 days [16]. Our study has revealed the use of steroids to be protective against stress hyperglycemia among critically ill patients within the first 48 hours of their critical illness and an increased risk of stress hyperglycemia after 48 hours. Steroid use at supraphysiological doses, reduces the synthesis of pro-inflammatory cytokines, T-cell function, and antibody Fc receptor expression, which activate anti-inflammatory and immunosuppressive processes, making them the mainstay in the treatment of numerous inflammatory diseases. While this remains true, the more gradual effects of steroids are those related to endocrine metabolism [25–28]. This is most likely the reason for the protective effect of steroids against patients with stress hyperglycemia within 48 hours and the increased risk of stress hyperglycemia thereafter.

The present study found that ICU mortality among patients with stress-hyperglycemia was higher (68.3%) compared to that of patients without stress hyperglycemia. Despite the fact that these results were higher compared to those reported by Sahin Temel *et al.*, Llompart-Pou *et al.,* and Rau *et al.,* which reported higher mortality rates of 20% [16], 13.3% [16,29,30] and 41.4% [2] respectively among patients with stress hyperglycemia as compared to those without stress hyperglycemia (5.6%), P= 0.05(52), (6.7%) (p=0.67) and 7.2% respectively [2,16,29] they all showed a similar association of higher mortality among patients with stress hyperglycemia compared to those without stress hyperglycemia. These differences could be due to a lack of protocols for the identification and treatment of stress hyperglycemia in our ICU for non-diabetic patients.

CONCLUSION

There is a high incidence of stress hyperglycemia among critically ill patients admitted in the ICU as evidenced in this study. Duration of ICU stay and comorbidities among patients admitted in medical and surgical ICU were found to be significantly associated with stress hyperglycemia. Steroid use was protective against stress hyperglycemia within first 48hours but a predictor of stress hyperglycemia after 48hours of ICU admission. Stress hyperglycemia contributes to higher mortality rate among critically ill patients.

Study limitation and recommendations

Follow-up time of the participants was short (30 days) in order to meet the deadline, set by the university for Mmed dissertations reports, therefore based on the results of this study we recommend long term follow up studies to be conducted in order to determine how many of patients with stress hyperglycemia will end up developing type 2 DM which is a common long-term complication among patients with stress hyperglycemia. We also recommend formulation of a protocol for monitoring and treating stress hyperglycemia in critically ill patients admitted in ICU who are non-diabetic in order to prevent and reduce the burden of morbidity and mortality resulting from stress hyperglycemia in critically ill patients in the ICU.

DECLARATION

Ethical approval and consent to participate this study was obtained from the Muhimbili University of Health and Allied Sciences (MUHAS) Research Ethics Committee with the certificate number MUHAS-REC-07-2021-771. The permission to correct data was obtained from the Management of Muhimbili National Hospital Upanga and Mloganzila campus where the study was conducted. A written informed consent for participating in the study was obtained from patients or their next of kin for those who were not able to give their consent. Participants who were not willing to continue with the study were permitted to drop out without any effect to the quality of care they receive at the health facilities. All participants received detailed information about the study. All patients with stress hyperglycemia were monitored and for those who had persistent hyperglycemia were treated according to the sliding scale available in the ICU protocol of DM management.

Consent for publication

Not Applicable.

Availability of data and materials

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

ADG conceived the study, collected data, analyzed the data and wrote the first draft of the manuscript. BJK and MM, assisted in data collection. GK, CM and ASA who assisted in data analysis. TN

and GS for their key role in guiding me throughout this study. All authors critically reviewed and approved the final version of the manuscript.

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