# EFFECT OF GLYCEMIC CONTROL ON SEPSIS IN CRITICALLY ILL DIABETIC PATIENTS: A PROSPECTIVE COHORT STUDY

Hatem Said Abdel Hamid, Amal Hamed Rabie, Michael Mamdouh Anwar and Samuel Habachi Daniel

#### **ABSTRACT:**

Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

#### **Corresponding author:**

Samuel Habachi Daniel Mobile: +2 01224394897 **E-mail:** samuel\_7abachi@hotmail.com

Received: 13/11/2023 Accepted: 10/02/2024

#### **Online ISSN: 2735-3540**

**Background:** In critically ill patients, hyperglycemia is common and frequently multifactorial. Severe hyperglycemia has been connected to negative outcomes in several conditions in non-diabetic patients. It can cause dysfunction of the endothelial system, release of cytokines, activation of platelets, dysfunction of the mitochondria, and disturbances in electrolytes and acid base balance. Diabetic patients have not shown these associations.

Aim of the Work: to study the effect of hyperglycemia in critically ill patients diagnosed with diabetes mellitus regarding the length of ICU or hospital stay and incidence of complications.

**Patients and Methods:** The current Prospective observational cohort study was conducted at hospitals of Ain-Shams University and the El Zeitoun Specialized Hospital. Sixty patients, all older than eighteen, who had been admitted to the intensive care unit due to sepsis and were known to have diabetes were enrolled in the study. Two groups of patients were randomly assigned: the first group's random blood glucose (RBG) measures were less than or equal to 150 mg/dl, and the second group's RBG measurements were greater than 150 mg/dl. Patients were assessed for clinical and laboratory parameters.

**Results:** patients in the second group, who had RBG level above 150mg/dl, had a significantly higher Acute Physiology and Chronic Health Evaluation (APACHEII) than the other group. Also, patients in the second group had a significantly longer hospital stay. On the other hand, both groups were comparable in sex, age, body mass index as well as special habits as smoking. The development of complications during ICU stay was similar in both groups.

**Conclusion:** Glycemic control in the ICU is a very import part in the management of ICU patients. Hyperglycemia is associated with higher APACHEII score and longer intensive care unit stay.

*Keywords: intensive care unit, glucose control, ICU, hyperglycemia, critically ill patients, Diabetic Patients.* 

#### **INTRODUCTION:**

Patients who are critically ill, frequently encounter hyperglycemia which is usually multifactorial. Severe hyperglycemia has been connected to negative outcomes in several conditions in non-diabetic patients. It can cause dysfunction of the endothelial system, release of cytokines, activation of platelets, dysfunction of the mitochondria, and disturbances in electrolytes and acid base balance. Diabetic patients have not shown these associations  $^{(1)}$ .

Reducing blood glucose (BG) levels by means of different measures has improved outcomes in some studies, but not all of them (2).In comparison to conventional management aimed at blood glucose (BG) 180 mg/dl. Numerous clinical trials conducted recently on critically ill patients have not demonstrated a decrease in mortality from intensive treatment focusing on neareuglycemia<sup>(3)</sup>.

On the other hands reports of hypoglycemia, which are frequently encountered and severe, are more harmful and leads to an increased rate in mortality among those critically ill patients <sup>(3)</sup>.

Mortality risk was significantly and independently encountered with a single hypoglycemic attack. Appropriate monitoring is necessary for secure execution of tight glycemic management in these critically ill patients in the intensive care unit (ICU) to decrease the risk of this consequence <sup>(4)</sup>.

## AIM OF THE WORK:

To study the effect of hyperglycemia in critically ill patients diagnosed with diabetes mellitus regarding the length of ICU or hospital stay and incidence of complications.

## **PATIENTS AND METHODS:**

This Prospective observational cohort study was conducted at hospitals of Ain Shams University and the El Zeitoun Specialized Hospital, throughout a period of 6 months on 60 patients that are known to be diabetic and admitted to ICU suffering from sepsis and aging over 18 years. These patients have fulfilled the following criteria:

## Inclusion Criteria:

All patients that are known diabetic and admitted to ICU suffering from sepsis aging over 18 years.

## Exclusion Criteria:

Age less than 18-year-old, patient or his 1st degree relatives refuses to participate and RBG level less than 70 mg/dl "on admission."

## **Study Groups:**

Considering inclusion and exclusion criteria, 60 Patients have been divided equally into two groups: 1st group RBG measurements less than or equal 150 mg/dl while the 2nd group RBG measurements above 150 mg/dl.

Demographic data which includes, age, gender, body mass index was collected for the studied patients, as well as the duration of diabetes and the site of the septic focus. Vital data as heart and respiratory rate, degree of temperature, blood pressure, oxygen saturation, central venous pressure and urine output were recorded for both studied groups. These patients were indicated to have hypertension if their systolic blood pressure (SBP) more than or equal to 140 mm Hg, their diastolic blood pressure (DBP) was greater than or equal 90 mm Hg, or if they were taking anti-hypertensive medication.

Laboratory data were divided into general and specific. The general tests included complete blood count (CBC), RBG, kidney and liver function tests, arterial blood gases (ABG) and hemoglobin A1C (HBA1C) level if available. The specific blood test included C reactive protein (CRP), lactate and lipid profile. The previous test when ordered were done with a maximum 5 ml blood sample per day. Accepted serum cholesterol levels were below 200mg/dl, otherwise patients were diagnosed to have hypercholesterolemia. Normal values of high-density lipoproteins (HDL) were above 50 mg/dl in females and 40mg/dl in males. As LDL density lipoproteins) for (low cholesterol as level below 70mg/dl in diabetic and cardiac patients was accepted.

Total insulin units needed per day according to body needs were recorded for each patient. RBG was recorded every hour if the patient was on insulin infusion, and every two hours after weaning from insulin infusion then every four hours while the patient was present in the ICU. Monitoring of glucose variability was recorded as an index about glycemic control. When blood glucose levels fell between 71 and 140 mg/dL, they were signified to be euglycemia; when they fell between 141 and 199 mg/dL, they were signified to be mild hyperglycemia; and when they fell above or equal to 200 mg/dL, they were classified as severe hyperglycemia.

Acute Physiology and Chronic Health Evaluation score II (APACHEII) It is calculated within a patient's first twenty-four hours in the critical care unit. Higher scores are indicative of greater risk of death and more severe illness. A score between 0 and 71 is calculated based on multiple parameters. The development of complications was noted for each patient in the current research; which includes Serum creatinine level (SCr) increase of 0.3 mg/dl within 48-hours; an elevation 1.5 times from the baseline, in the previous 7 days; or a urine volume of 0.5 ml/kg/h for 6 hours were all considered signs of acute kidney injury (AKI). Pyuria, which is described as having 10 or more white blood cells per cubic millimeters in a urine sample. Acute respiratory distress syndrome (ARDS) onset, the necessity of mechanical ventilation, and its duration, acute myocardial infarction, strokes were noted, as well as the duration of the ICU stay.

#### **Primary Outcome Measurement:**

Evaluate the effect of hyperglycemia on APACHE score calculation and the length of ICU stay in diabetic critically ill patients.

## **Ethical Consideration**:

Approvals of anesthesia and intensive care department and the research ethics committee, faculty of medicine, Ain Shams university were obtained before starting study the [MS102/2021] Prior to their enrollment in the study, every patient provided written, informed consent.

## **Statistical Analysis of The Data:**

The computer was fed data, and IBM SPSS software package version 20.0 was employed for analysis. (IBM Corp., Armonk, NY) Numbers and percentages for qualitative data. The Kolmogorov-Smirnov test was used to confirm the distribution's normality. Range mean, standard deviation, median, and interquartile range (IQR) for quantitative data. The results were deemed significant at the 5% level, p<0.05. The tests employed were Chi-square test: To compare different groups based on categorical variables. When the expected count is less than 5 in more than 20% of the cells, the chi-square needs to be corrected using Fisher's Exact. Student t-test for quantitative variables that are normally distributed. Mann Whitney to compare when quantitative variables have an abnormal distribution.

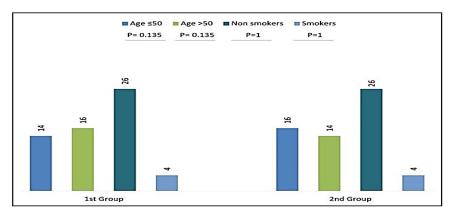
## **RESULTS:**

Thirty patients were included in each group with comparable demographic data as regards age, sex and special habits (smoking), as well as body mass index. Table (1&2), Diagram (1).

Table 1: Comparison of demographic data between the two studied groups.

Demographic data	$1^{st} Group$ RBG $\leq 150 \text{ mg/dl}$ (n = 30)		$2^{nd}$ Group RBG >150 mg/dl (n = 30)		Test of Sig.	р
	No.	%	No.	%		
Sex						
Male	18	60.0	16	53.3	2 0.271	0.602
Female	12	40.0	14	46.7	$\chi^2 = 0.271$	
Age (years)						
≤50	14	46.7	16	53.3	2 1 450	0.13
>50	16	53.3	14	46.7	$\chi^2 = 1.456$	
Special habits						
Non-smoker	26	86.7	26	86.7	2 0.00	1.000
Smoker	4	13.3	4	13.3	$\chi^2 = 0.00$	1.000

RBG: random blood glucose,  $\chi^2$ : Chi square test.



**Diagram 1:** Comparison of demographic data between the two studied groups **Table 2:** Comparison of BMI between the two studied groups.

BMI (kg/m2)	$\begin{array}{c} 1^{st} \mbox{ Group} \\ RBG \leq 150 \mbox{ mg/dl} \\ (n = 30) \end{array}$		$2^{nd} Group RBG >150 mg/dl (n = 30)$		Test of Sig.	р
	No.	%	No.	%		
Normal (18.5-24.9)	30	100	30	100	χ²=0.0	1
Min. – Max.	17.50 -	24.70	16.0 -	- 24.20	T_1 94	0.0607
Mean ± SD.	22.84 ±	1.52	21.22	± 1.34	T=1.84	0.0697

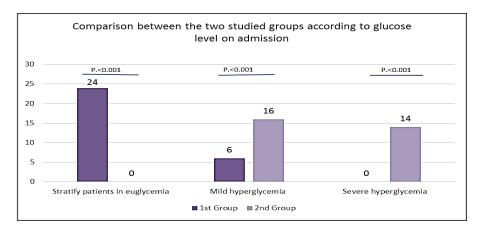
RBG: random blood glucose, BMI: body mass index, min: minimum, max: maximum, SD: standard deviation,  $\chi^2$ : Chi square test, t: Student t-test, SD: Standard deviation.

A statically significant difference was found between both groups as regards the glucose level on admission. The first group has a significant increase in the number of patients, whose RBG level were between 71 and 140 mg/dl (80% vs. 0% respectively p<0.001). The second group showed a significant higher percentage of patients when the RBG was between 141 and 199 mg/dl (53.3 % vs. 20% respectively p<0.001) and above or equal 200 mg/dl than the other group (46.7% vs. 0% respectively p<0.001) Table (3) and Diagram (2). Vital data and risk factors were comparable in both groups on admission (p >0.05) Table (4 &5), Diagram (3).

Table 3: Comparison between both groups as regards glucose level on admission.

Glucose level on admission	$1^{st} Group$ RBG $\leq 150 \text{ mg/dl}$ (n = 30)		$2^{nd}$ Group RBG >150 mg/dl (n = 30)		Test of sig.	р	
	No.	%	No.	%			
Stratify patients in euglycemia. (71-140)	24	80.0	0	0.0			
Mild hyperglycemia (141-199)	6	20.0	16	53.3	$\chi^2 = 42.545*$	< 0.001*	
Severe hyperglycemia (≥200)	0	0.0	14	46.7			

RBG: random blood glucose,  $\chi^2$ : Chi square test



**Diagram 2:** Comparison between both groups according to glucose level on admission. **Table 4:** Comparison between the two studied groups according to vital data on admission.

	1st Group	2 <sup>nd</sup> Group		
Vital data	$RBG \le 150 \text{ mg/dl}$	RBG >150 mg/dl	t	р
	(n = 30)	(n = 30)		
Systolic blood pressure (mmHg)				
Range	120.0 - 140.0	115.0-135.0	1.259	0.213
Mean $\pm$ SD.	$132.33 \pm 19.60$	$139.0\pm21.39$	1.239	0.215
Diastolic blood pressure (mmHg)				
Range	65.0 - 85.0	70.0 - 85.0	1.527	0.132
Mean $\pm$ SD.	$82.33 \pm 11.35$	$87.33 \pm 13.88$	1.327	0.152
Mean arterial blood pressure (mmHg)				
Range	83.0 - 120.0	83.0 - 130.0	1.480	0.144
Mean $\pm$ SD.	$99.0 \pm 13.31$	$104.56\pm15.66$	1.480	0.144
Temperature (°C)				
Range	36.2 - 37.7	36.3 - 37.8	0.836	0.407
Mean $\pm$ SD.	$38.08 \pm 0.68$	$37.94 \pm 0.54$	0.830	0.407
Heart rate (beat/ min)				
Range	90.0 - 110.0	92.0 - 112.0	1.483	0.144
Mean $\pm$ SD.	$106.47 \pm 10.87$	$106.47 \pm 10.87$ $101.83 \pm 13.22$		0.144
Respiratory rate (breath/ min)				
Range	16.0 - 28.0	24.0 - 29.0	0.024	0.081
Mean ± SD.	$20.0 \pm 5.14$	$20.03 \pm 5.77$	0.024	0.981
DDG 1 11 1 1			a 1 '	

RBG: random blood glucose, t: Student t-test, SD: Standard deviation, °C: degree Celsius

Table 5: Comparison between both groups according to risk factors.

Risk Factors	$1^{st}$ Gr RBG $\leq 15$ (n = 1)	i0 mg/dl	$2^{nd} Group$ RBG >150 mg/dl (n = 30)		$\chi^2$	р
	No.	%	No.	%		
Hypertension	11	36.7	12	40.0	0.071	0.791
Neuropathy	8	26.6	5	16.7	0.131	1.000
Hyperlipidemia	6	20.0	11	36.7	3.068	0.080
Smoking	5	16.6	2	6.6	0.373	0.542

RBG: random blood glucose,  $\chi 2$ : Chi square test

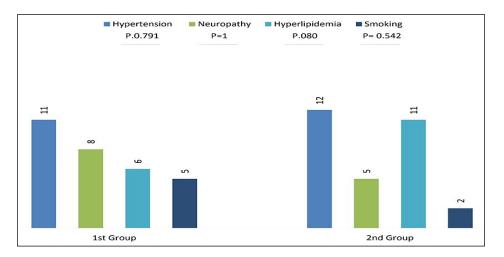


Diagram 3: Comparison between both groups according to risk factors.

The APACHEII score was significantly higher in the second group than the first group (mean $\pm$  SD 10 $\pm$ 1.3 vs. 9 $\pm$ 1.2 respectively

p=0.003). As regards the CRP and lactate, there was no significant difference between both groups Table (6).

Cable 6: Comparison between both groups according to laboratory investigations (CRP and Lactate)	) and
APACHEII score.	

	$\begin{array}{c} 1^{st} \mbox{ Group} \\ \mbox{RBG} \leq 150 \mbox{ mg/dl} \\ \mbox{ (n = 30)} \end{array}$	$2^{nd} Group$ RBG >150 mg/dl (n = 30)	t	Р
CRP				
Range	0 –5	2-10	2 221	0.0656
Mean ± SD.	$5.94 \pm 1.85$	$6.11 \pm 1.09$	2.231	0.0656
Lactate				
Range	0.5 - 2	0.5 - 2	1.912*	0.061
Mean $\pm$ SD.	$1.50\pm0.60$	$1.85\pm0.81$	1.912*	0.061
APACHEII score				
Range	7 - 11	7-12	2.000	0.002*
Mean ±SD	9 ±1.2	10±1.3	-3.096	0.003*

RBG: random blood glucose, CRP: c reactive protein, APACHEII: Acute Physiology and Chronic Health Evaluation score II, SD: Standard deviation t: Student t-test.

The duration of ICU stay was significantly higher in the second group than the first group with median and interquartile range 4.0 (3.0-7.0) vs. 4.0 (3.0-5.0) respectively p=0.0341 Table (7).

Diagram (5) also shows the comparison between the 2 groups regarding hospital stays in relation to blood sugar level.

There was no significant difference in the

development of complications (Acute kidney injury, Acute coronary syndrome, chest infection and pyuria) during ICU stay between both groups. Table (8), Diagram (4). There was a statistically significant increase of mean blood glucose in second group in comparison to first group on days 2,3,4,5 and 6 (P.<0.05).

 Table 7: Comparison between both groups according to ICU Length of stay from admission till discharge.

	$1^{st}$ Group RBG $\leq 150$ mg/dl (n = 30)	$2^{nd}$ Group RBG >150 mg/dl (n = 30)	Test of sig.	Р
ICU length of stay in days				•
Range	2.0 - 6.0	2.0 - 8.0	U = 612.50	0.0241*
Median (IQR)	4.0 (3.0 - 5.0)	4.0 (3.0 - 7.0)	U= 613.50	0.0341*
· · · DDC 1	11 1 1 10	N T	<b>TT NG TT</b>	

ICU: intensive care unit, RBG: random blood glucose, IQR: Inter quartile range U: Mann Whitney test.

Table 8: Comparison between both groups according to the development of complications.

Complications	$RBG \leq$	Group 150 mg/dl = 30)	RBG >1	Group 150 mg/dl = 30)	$\chi^2$	р
	No.	%	No.	%		
Acute kidney injury	2	3.3	4	13.0	0.218	1.000
Acute coronary syndrome	0	0.0	2	3.3	3.158	0.237
Chest infection	2	3.3	3	10.0	0.00	1.000
Pyuria	3	10.0	4	13.0	0.00	1.000

RBG: random blood glucose,  $\chi^2$ : Chi square test

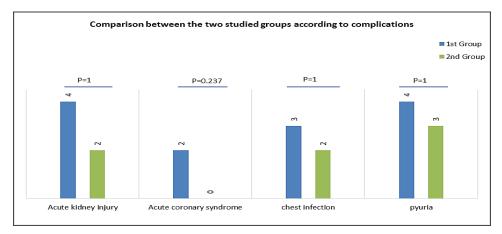


Diagram 4: Comparison between the two studied groups as regards the development of complications

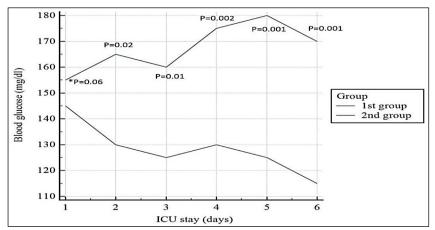
Table 9: Comparison between both groups according to blood glucose in relation toICU stay

	Mean bloc		
ICU stay (days)	1 <sup>st</sup> Group	2 <sup>nd</sup> Group	Р
	$RBG \le 150 \text{ mg/dl}$	RBG >150 mg/dl	Г
	(n = 30)	(n = 30)	
First Day	145	155	0.0632
Second Day	130	165	0.0234*
Third Day	125	160	0.0125*
Fourth Day	130	175	0.0023*
Fifth Day	125	180	0.00167*
Sixth Day	115	170	0.00113*

RBG: random blood glucose.

This table shows that there was statistically significant increase of mean

blood glucose in second group in comparison to first group at day 2,3,4,5 and 6 (P.<0.05).



**Diagram 5:** Comparison between both groups according to blood glucose in relation to ICU stay.

#### **DISCUSSION:**

Diabetes mellitus (DM) patients still have a worse prognosis following ischemic episodes than those without diabetes, despite advancements in DM patient care. Critically ill patients in the intensive care unit, most commonly encounter hyperglycemia. whatever the cause for admission (sepsis, acute myocardial infarction, stroke, post cardiovascular surgery, etc.), is the occurrence of hyperglycemia is linked to increased mortality and morbidity<sup>(5)</sup>.

Nonetheless, there is ongoing debate regarding the pathophysiology and, specific ally, the management of hyperglycemia in critically ill patients. A blood glucose level more than 140 mg/dL without a prior history of diabetes or a glycated hemoglobin (HbA1c) more than 6.5% is referred to as stress hyperglycemia which is frequently encountered in the ICU. Even when there is no prior history of diabetes mellitus, stress hyperglycemia is considered a prevalent issue among critically ill patients and is linked to higher rates of mortality and morbidity <sup>(6)</sup>.

The literature shows conflicting results regarding the target for maintaining glucose level in these patients and its relation to the patient's short-term outcome. According to some data, hyperglycemia, at 180 mg/dL, is linked to an increased risk of infection-related death and morbidity in intensive care unit patients. On the other hand, in comparison to conventional management aimed at BG 180 mg/dl, several current clinical trials involving patients who are critically ill have not shown a decrease in mortality when maintaining euglycemia<sup>(7)</sup>.

Considerable harm is encountered in events of severe hypoglycemia, which also leads to increased mortality <sup>(3)</sup>. Since a single severe hypoglycemic episode was linked to an increased risk of death on its own. To lower the risk of this happening, safe tight glycemic control implementation necessitates proper monitoring <sup>(8)</sup>.

Therefore, managing glucose in the intensive care unit is very important during the daily management of a patient that is extremely complex. The purpose of the present study is to assess the effects of glycemic control in critically ill diabetic patients, even though observational and some interventional trials said that strict glucose management can lower mortality in this context. However, more evident research has not supported these findings.

In our current study patients, there that were included were comparable in both age sex and BMI. On the contrary, research has demonstrated that older patients had higher level of hyperglycemia and there was a substantial correlation between age and the occurrences of complications and death<sup>(9)</sup>. Also, there was no difference in smoking between both groups and this was in accordance with *Lou et al*  $^{(3)}$ .

The Acute Physiology and Chronic Health Evaluation (APACHEII) in our current study revealed a significant increase in the higher hyperglycemia group. In line with our research, *Cichosz and Schaarup* reported that the APACHE score was higher in the two groups with hyperglycemia than in the non-hyperglycemia groups. This contradicts the findings of *Lou et al.* (2021), who found no statistically significant relationship between the APACHE II score and e, ither the maximum glucose level within first 2 days or the admission glucose level.

In the current study, there was statistically insignificant difference between both groups in vital data (Systolic BP, Diastolic BP, MABP, HR and RR) (P.>0.05). However, hemodynamic parameters, the presence of risk factors, and comorbidities indicated that patients with hyperglycemia had decreased systolic and diastolic BP as demonstrated in Hassan et al., (2021) study <sup>(10)</sup>. These findings corroborated those of Pandey et al., (2014), who discovered that there was an increase in variability in both systolic and diastolic BP values in patients with hyperglycemia and sepsis, which increased as the severity of the disease worsened. Additionally, they discovered a positive relation between the variability in systolic and the diastolic blood pressure and the APACHE II score<sup>(11)</sup>

*Moreover, Abd El-Monem et al., (2021)* was in agreement with our study as the insignificant difference in respiratory rate and ABG between both groups<sup>(12)</sup>. *Ganesh et al., (2016)* provided an explanation for these results, stating that high anion gap metabolic acidosis, as well as lactate, is the predominant blood gas anomaly in patients having sepsis and septic shock. But lactate was also similar in both groups in our study<sup>(13)</sup>.

In our study, there was similar CRP measurements in both groups. On the contrary, *Hassan et al.*, (2021) revealed a significant elevation in CRP in the

hyperglycemia group than the other group. Inflammatory markers like c reactive protein have been linked to type 2 diabetes mellitus and insulin resistance, according to a 2009 study by *Sourris et al.* Additionally, *Ford et al.*, had demonstrated that individuals without diabetes have higher HbA1c levels and that those with diabetes have higher CRP levels <sup>(14)</sup>.

The length of intensive care unit stay was significantly increased in the higher hyperglycemia group than the other group. This is equivalent to the findings of Abd El-Monem et al., (2021), who demonstrated a statistically significant elevation in the length intensive care stav of unit in the hyperglycemia group relative to the other group. In support of the previous findings, Marik and Bellomo (2013) noted that patients with stress hyperglycemia had longer intensive care unit and hospital stays. They proceeded on to state that because severe hyperglycemia affects stress serum osmolarity, it could be dangerous Severe hyperglycemia also surpasses the renal threshold, which causes volume depletion and osmotic diuresis<sup>(15)</sup>.

In line with the aforementioned, *Lou et al.*, (2021) reported that moderate and severe hyperglycemia was associated with a marked longer admission in the intensive care unit when compared to the normoglycemic group, based on the peak glucose level forty-eight hours after admission <sup>(6)</sup>.

This aligns with the views of *Temel etal.* and Callahan and Supinski, who demonstrated that hyperglycemia was a grave element for weakness obtained in the intensive care unit that extended the need for mechanical ventilation <sup>(8)</sup>. Additionally, *Becker et al.* discovered a significant correlation between an increased ICU and hospital stay and suboptimal hyperglycemic control more than 180 mg/dl) in the intensive care unit stay <sup>(16)</sup>.

Similar to our findings, *Cichosz et al.'s* study found that the length of ICU stay was longer for patients with hyperglycemia than for those without. This suggests that patients

with diabetes have longer ICU stays than patients without hyperglycemia, but the effect is less pronounced <sup>(9).</sup>

The current study revealed an insignificant difference in complications between both groups. while in *Cichosz and Schaarup, 2017* the mortality rate among intensive care unit patients with diabetes was higher than controls.

In this concern, *El-Nagar and colleagues* (2018) showed that there was a significant link between HbA1c and mortality; the higher the HbA1c, the higher the mortality. This agrees with the study by *Mahmoodpoor* et al. who reported the same result and confirmed the association between higher HbA1c and the incidence of higher mortality and complication. Moreover, in the study by El-Nagar and colleagues (2018) there was a significant relationship between RBS and mortality rate. This is in agreement with the study by Mahmoodpoor and colleagues (2008), who reported the same result and also confirmed the association between the RBS and increased mortality (20&21).

*El-Nagar et al. (2018)* demonstrated a noteworthy relation between HbA1c and mortality, indicating that an elevation in HbA1c corresponded to an increase in mortality. This is consistent with the research conducted by *Mahmoodpoor et al.*, who also found a correlation between higher HbA1c and an increased risk of death and complications <sup>(20&21)</sup>.

Furthermore, *El-Nagar and colleagues'* (2018) study found a significant correlation between RBG and mortality rate. This is consistent with the research conducted in 2008 by *Mahmoodpoor et al.*, who also reported the same outcome and verified the link between higher mortality and RBS <sup>(20, 21)</sup>.

Taking complications into account, a cohort of patients receiving intensive glucose control between 80 and 140 mg/dL) studied the relation between glucose management and sepsis severity. The researchers

concluded that there was a higher risk of hypoglycemia and hyperglycemia in those with high degree of sepsis or septic shock <sup>(17)</sup>.

The Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis (VISEP study) was a randomized multi-center trial that compared intensive versus conservative insulin therapy. Additionally, the fluids (10% pentastarch vs. modified Ringer's lactate) were studied for resuscitation. Strict glucose management did not help patients with high degree of sepsis, and the trial was early terminated for safety concerns due to elevated incidence of hypoglycemia<sup>(18)</sup>.

An examination of subgroups in the NICE-SUGAR trial revealed no improvement in the mortality rate for patients with high degree of sepsis. According to the Surviving Sepsis Campaign Guidelines, insulin therapy should be initiated following two following blood glucose readings above 180 mg/dL<sup>(19)</sup>.

According to *El-Nagar et al.'s* (2018) multivariate regression analysis, the most independent risk factors for mortality in critically ill patients were HbA1c, stroke, and renal disease. This is consistent with the findings of a study by *Bonora et al.*, which also confirmed that the most independent risk factors for mortality in ICU were higher HbA1c, renal disease, and stroke. Hyperglycemia was not among those factors <sup>(22)</sup>.

The absence of significant in the development of complications between both groups can be due to the small sample size used. So, additional observational and randomization and controlled studies are recommended to be performed for additional evaluation of the development of complications with different levels of hyperglycemia.

## **Conclusion:**

Glycemic control in the intensive care unit is a very import part in the management of ICU patients. Hyperglycemia is associated with higher APACHEII score and longer intensive care unit stay.

#### **Conflict of interest and funding:**

No conflict of interest existed, and the research received no funding from any sources.

#### **REFERENCES:**

- Dungan KM, Braithwaite SS, Preiser JC. 2009: Stress hyperglycaemia. Lancet. 23; 373 (9677):1798-807. doi: 10.1016/S0140 – 6736 (09)60553-5. PMID: 19465235; PMCID: PMC3144755.
- De La Rosa Gdel, C., Donado, J. H., Restrepo, A. H., Quintero, A. M., González, L. G., Saldarriaga, N. E., & Arango, C. M. (2008). Grupo de Investigacion en Cuidado intensivo GICI-HPTU: Strict glycaemic control in patients hospitalised in a mixed medical and surgical intensive care unit: a randomised clinical trial. Crit Care, 12 (5), R120-R120.
- 3. Nice-Sugar Study Investigators. (2009). Intensive versus conventional glucose control in critically ill patients. New England Journal of Medicine, 360 (13), 1283-1297.
- 4. **Krinsley, J. S., & Grover, A. (2007).** Severe hypoglycemia in critically ill patients: risk factors and outcomes. Critical care medicine, 35(10), 2262-2267.
- Robba, C., & Bilotta, F. (2016). Admission hyperglycemia and outcome in ICU patients with sepsis. *Journal of Thoracic Disease*, 8(7), E581–E583.
- Lou, R., Jiang, L., & Zhu, B. (2021). Effect of Glycemic Gap upon Mortality in Critically Ill Patients with Diabetes. *Journal of Diabetes Investigation*. 1852 (5), 873-881.
- 7. Corsino, L., Dhatariya, K., & Umpierrez, G. (2015). *Management of diabetes and hyperglycemia in hospitalized patients*. Clinical immunology, 44 (7), 1338–1346.
- Temel, S., Yuksel, R. C., Gundogan, K., Ulgey, A., Guven, M., & Sungur, M. (2018). Stress Hyperglycemia Incidence in Critically Ill Patients: Cross-Sectional Observational Study/Kritik Hastalarda Stres Hiperglisemi Sikligi: Tanimlayici Kesitsel

Calisma. Dahili ve Cerrahi Bilimler Yoğun Bakım Dergisi (Journal of Medical and Surgical Intensive Care Medicine), 9(2), 46– 51.

- 9. Cichosz, S. L., & Schaarup, C. (2017). Hyperglycemia as a Predictor for Adverse Outcome in ICU Patients With and Without Diabetes. *Journal of Diabetes Science and Technology*, 11(6), 1272–1273.
- Hassan. Badr, G Al-Ashker, A, & A. Ahmed, A. (2021). Admission Hyperglycemia in Critically Ill Patients with Sepsis in Medical Icu; Role of Insulin Resistance and Its Relation to Outcome. *Al-Azhar Medical Journal*, 50(1), 577–590.
- 11. **Pandey N, Bian, Y., & Shou, S. (2014).** Significance of blood pressure variability in patients with sepsis. *World Journal of Emergency Medicine*, *5*(1), 42-53.
- Abd El-Monem, D., A Badr, G., & Ahmed, A. (2021). Admission Hyperglycemia in Critically Ill Patients with Sepsis; High Il6 and Its Relation With Outcome. Al-Azhar Medical Journal, 50(2), 1305-1316.
- Ganesh K., Sharma, R., Varghese, J., & Pillai, M. G. K. (2016). A profile of metabolic acidosis in patients with sepsis in an Intensive Care Unit setting. *International Journal of Critical Illness and Injury Science*, 6(4), 178-180.
- 14. Sourris K, Lyons, J. de Courten, M. P. J., Dougherty, S. L., Henstridge, D. C., Cooper, M. E., Hage, M., Dart, A., Kingwell, B. A., & Forbes, J. M. (2009). c-Jun NH2-terminal kinase activity in subcutaneous adipose tissue but not nuclear factor-κB activity in peripheral blood mononuclear cells is an independent determinant of insulin resistance in healthy individuals. *Diabetes*, 58(6), 1259–1265.
- 15. Marik, P. E., & Bellomo, R. (2013). Stress hyperglycemia: an essential survival response! *Critical Care*, *17* (2), 305
- Becker, C. D., Sabang, R. L., Cordeiro, M. F. N., Hassan, I. F., Goldberg, M. D., & Scurlock, C. S. (2020). Hyperglycemia in medically critically ill patients: risk factors and clinical outcomes. The American journal of medicine, 133(10), e568-e574.
- 17. Waeschle, R. M., Moerer, O., Hilgers, R.,

Herrmann, P., Neumann, P., & Quintel, M. (2008). The impact of the severity of sepsis on the risk of hypoglycaemia and glycaemic variability. *Critical Care (London, England)*, *12*(5), R129.

- Dellinger, R. P., Levy, M. M., Rhodes, A., Annane, D., Gerlach, H., Opal, S. M., Sevransky, J. E., Sprung, C. L., Douglas, I. S., Jaeschke, R., Osborn, T. M., Nunnally, M. E., Townsend, S. R., Reinhart, K., Kleinpell, R. M., Angus, D. C., Deutschman, C. S., Machado, F. R., Rubenfeld, G. D., ... Moreno, R. (2013). Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Critical Care Medicine, 41 (2), 580–637.
- Viana, M. V., Moraes, R. B., Fabbrin, A. R., Santos, M. F., & Gerchman, F. (2014). Assessment and treatment of hyperglycemia in critically ill patients TT - Avaliação e tratamento da hiperglicemia em pacientes graves. *Revista Brasileira de terapia*

intensiva, 26 (1), 71-76.

- El-Nagar, M. G., El-Raouf, M. A., El-Dien, W. S., Nooh, M. Z., & Tawfiek, A. S. (2018). Study of hyperglycemia in critically ill patients and its impact on the outcome. *Menoufia Medical Journal*, 31(3), 935.
- 21. Mahmoodpoor, A., Hamishehkar, H., Shadvar, K., Beigmohammadi, M., Iranpour, A., & Sanaie, S. (2016). Relationship between glycated hemoglobin, Intensive Care Unit admission blood sugar and glucose control with ICU mortality in critically ill patients. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine, 20(2), 67-77.
- Bonora, E., Kiechl, S., Mayr, A., Zoppini, G., Targher, G., Bonadonna, R. C., & Willeit, J. (2011). High-normal HbA1c is a strong predictor of type 2 diabetes in the general population. Diabetes care, 34(4), 1038-1040.

تأثير التحكم في نسبة السكر في الدم على تسمم الدم لدى مرضى السكري المصابين بأمراض خطيرة ( دراسة أترابية مستقبلية )

حاتم سعيد عبد الحميد وأمل حامد ربيع ومايكل ممدوح أنور وصموئيل حبشي دانيال

قسم التخدير و الرعايه المركزه و علاج الالم - كليه الطب جامعه عين شمس

**الخلفيه العلميه**: رتفاع السكر في الدم أمر شائع وغالباً ما يكون متعدد العوامل في المرضى المصابين بأمراض خطيرة. يمكن أن يؤدي ارتفاع السكر في الدم الشديد إلى خلل في بطانة الأوعية الدموية، وإطلاق السيتوكين، وتنشيط الصفائح الدموية، وخلل في الميتوكوندريا، واضطرابات الكهارل والقواعد الحمضية، وقد ارتبط بنتيجة ضارة في مجموعة متنوعة من الإعدادات لدى المرضى الذين ليس لديهم تاريخ من مرض السكري. ولم يتم إثبات هذا الارتباط لدى مرضى السكري.

**المرضي المشتركين و الوسائل**: تم إجراء هذه الدراسة الأترابية في مستشفيات جامعة عين شمس - مستشفى الزيتون التخصصي. 60 مريضًا معروفًا بمرض السكري وتم إدخالهم إلى وحدة العناية المركزة يعانون من تعفن الدم الذين تزيد أعمار هم عن 18 عامًا. تم تقسيم المرضى بالتساوي إلى مجموعتين: قياسات المجموعة الأولى أقل من او يساوي 150 ملجم/ديسيلتر بينما قياسات المجموعة الثانية أعلى من 150 ملجم/ديسيلتر.

النتائج: تبين وجود تباين احصائي للبقاء في وحدة العناية المركزة في المجموعة الثانية، مقارنة بالمجموعة الأولى.

**الخاتمه**: ارتبط ارتفاع السكر في الدم بزيادة مدة إجمالي الأيام في وحدة العناية المركزة. كانت هناك زيادة غير معنوية في الحالات المعقدة في مجموعة ارتفاع السكر في الدم مقارنة بالمجموعة الأخرى. قد يكون هذا بسبب قلة عدد المرضى في دراستنا. لذلك يُقترح إجراء المزيد من دراسات المراقبة والمراقبة العشوائية لمزيد من تقييم تباين المضاعفات.