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Original Article

Can we Provide Effective Glycemic Control in Intensive Care Unit? Point Prevalence Study

Yeliz Bilir,[1] Yekbun Bulun,[1] Fulya Ciyiltepe,[2] Kemal Tolga Saraçoğlu[3]

[1]Department of Anesthesiology and Reanimasyon, Intensive Care Unit, Health Sciences University, Kartal Dr. Lutfi Kirdar City Hospital, İstanbul, Türkiye
[2]Department of Intensive Care Unit, Antalya Training and Research Hospital, Antalya, Türkiye
[3]Department of Anesthesiology and Reanimasyon, Hamad General Hospital, Doha, Qatar

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Correspondence: Yeliz Bilir, Kartal Dr. Lutfi Kirdar City Hospital, İstanbul, Türkiye
E-mail: dryelizbilir@yahoo.com

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ABSTRACT

Objective: Blood glucose dysregulation is independently associated with mortality and morbidity in critically ill patients. However, it is difficult to keep glycemic control at targeted levels in diabetic and non-diabetic patients in intensive care units (ICU). A point prevalence study was planned to evaluate glycemic control in patients treated in the tertiary ICU. Ethics committee approval was obtained before starting the study.

Methods: The demographic data of the patients, their characteristics at the time of admission, intensive care follow-up and treatment, the nutrition method, and the parameters related to glycemic control were recorded.

Results: On the study day, a total of 107 patients, 35 of whom were COVID (C-ICU) and 72 were in the non-Covid ICU (NC-ICU), were included in the study. 47.6% of the patients were male and 29.9% had a diagnosis of diabetes mellitus (DM). The mean blood glucose value of the patients was measured as 158 mg/dL and glycemic dysregulation (4.7% hypoglycemia and 25.2% hyperglycemia) was detected in 29.9% of all patients. Blood glucose levels were unregulated in 28.6% (n=10) of the patients in C-ICU and 30.5% (n=22) patients in NC-ICU. The patients with regulated blood glucose were similar between the two groups (p=0.510). A statistically significant correlation was found between the patients' unregulated blood glucose levels and the presence of DM (p=0.05).

Conclusion: The idea that a certain glucose target may not always be optimal for all patients and that individualized glucose control is currently being discussed. We believe that blood glucose algorithms are necessary in ICUs without putting patients into hypoglycemia or hyperglycemia in routine follow-up.

INTRODUCTION

Blood glucose regulation, hyperglycemia, and hypoglycemia are important problems we encounter in intensive care units (ICU). Hyperglycemia disrupts the metabolic balance of the patients and has a negative impact on the healing process. Apart from metabolic disorders, hyperglycemia delays the recovery time of clinical manifestations such as bloodstream infections and decubitus. In addition, it causes adverse side effects such as deterioration in fluid balance, immunosuppression, increased inflammation, impaired leukocyte functions, a tendency to thrombosis, and endothelial dysfunction.[1,2] Hypoglycemia, on the other hand, causes dysfunction of vital organs, especially the brain and heart.[3,4] Cardiac arrhythmia and/or infarction due to insufficient nutrition of the myocardium and a transient ischemic attack in the brain are important undesirable conditions. Diabetes mellitus (DM) is one of the most diagnosed comorbidities in patients admitted to the ICU. Hyperglycemia that develops during the follow-up of inpatients may be due to diabetes as well as non-diabetic causes. "Stress hyperglycemia" is one of the common causes of hyperglycemia in non-diabetic patients.[5] In healthy individuals, plasma glucose levels are kept in a very narrow range by the release of insulin and counter-regulatory hormones (glucagon, epinephrine, cortisol, and growth hormone). In stressful situations, there is an increase in counter-regulatory hormones, which increase hepatic glucose production and decrease glucose utilization by peripheral tissues, causing hyperglycemia.[1] Stress hyperglycemia develops due to stress during acute illness, and blood glucose returns to normal after the cause of stress is eliminated.

There are many factors that increase the susceptibility to hyperglycemia in intensive care patients; use of vasopressor agents, enteral and parenteral nutrition, glucose-con-

taining IV infusions, immobilization, and steroid use.[6] In the literature, there are many studies showing that hyperglycemia in intensive care patients is a major risk factor for increased morbidity and mortality.[7-9] For this reason, the necessity of strict glycemic control (110–140 mg/dL) in ICUs has been emphasized for a long time. However, because of this, hypoglycemia attacks started to be seen more frequently, and there was feedback on this issue.[3,4] A major study was started in 2009, and it changed the perspective on the necessity of tight glycemic control. In the NICE-SUGAR study, it was shown that strict glycemic control adversely affected mortality and even increased mortality (17%) due to episodes of hypoglycemia.[10]

As a result, it is important to prevent the occurrence of hyperglycemia and hypoglycemia and to treat them early when they develop. In this study, we aimed to determine the blood glucose regulation status of the patients in the ICUs of our hospital by performing a point prevalence study. A secondary outcome was to increase our clinical awareness and evaluate our own approach.

MATERIALS AND METHODS

Data Collection

The study was conducted in the 140-bed Anesthesiology and Reanimation ICU. ICUs consist of nine units, one of which is the COVID ICU. The protocol was approved by the Dr Lutfi Kırdar Training and Research Hospital Ethics Committee [2022/514/218/32]. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients, who were hospitalized in the ICU for more than 24 h, were over 18 years old, were not pregnant, had no brain death, and were hospitalized for reasons other than acute complications of diabetes (diabetic ketoacidosis, hypoglycemia, and nonketotic hyperosmolar hyperglycemic coma) were included in the study. Data were collected from the computer-based patient registry system and patient files.

Variables of interest included demographic variables (age, gender), reasons for admission, illness severity on admission Acute Physiology and Chronic Health Evaluation-APACHE II- score and Sequential Organ Failure assessment-SOFA-score in the first 24 h in the ICU, length of stay, and advanced clinical interventions received in the ICU (vasoactive medications, mechanical ventilation, continuous renal replacement therapy [CRRT]).

Variables of interest are patients' blood glucose level monitoring included presence of DM, use of steroid, inotropic, and insulin therapy, dietary patterns, the highest and lowest blood glucose levels on the working day, the number of patients with hypoglycemia (<60 mg/dL) on that day, the number of patients with hyperglycemia (>180 mg/dL) and the total number of dysregulated patients.

The Design and Setting of the Study

There are several rules we pay attention to and an "insulin protocol" we apply to ensure glucose monitoring and regulation in the ICU. All patients' blood glucose values are kept between 140 and 180 mg/dL. These values were determined based on the Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, the American Association of Clinical Endocrinologists and American Diabetes Association consensus report, and the NICE-SUGAR trial of the Surviving Sepsis Campaign.[10-12]

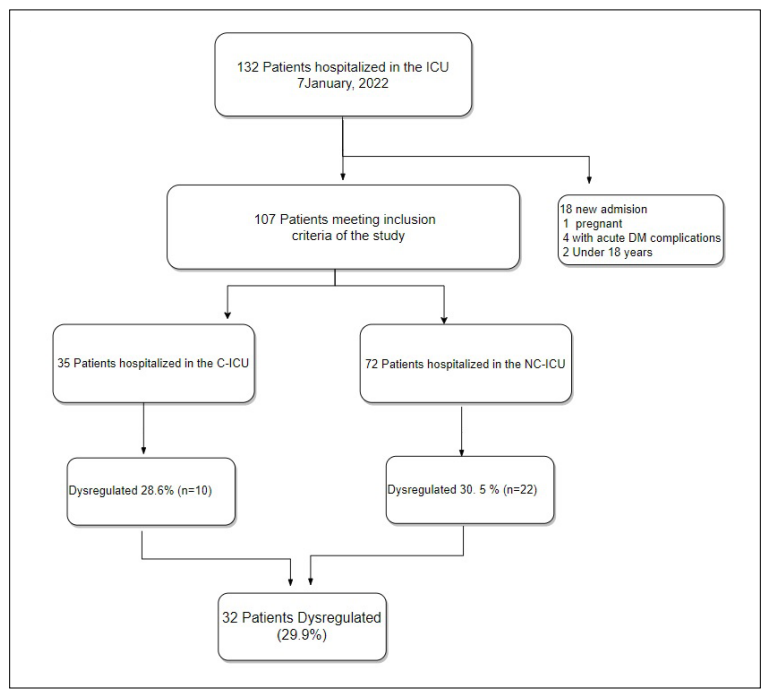

Figure 1. Flowchart

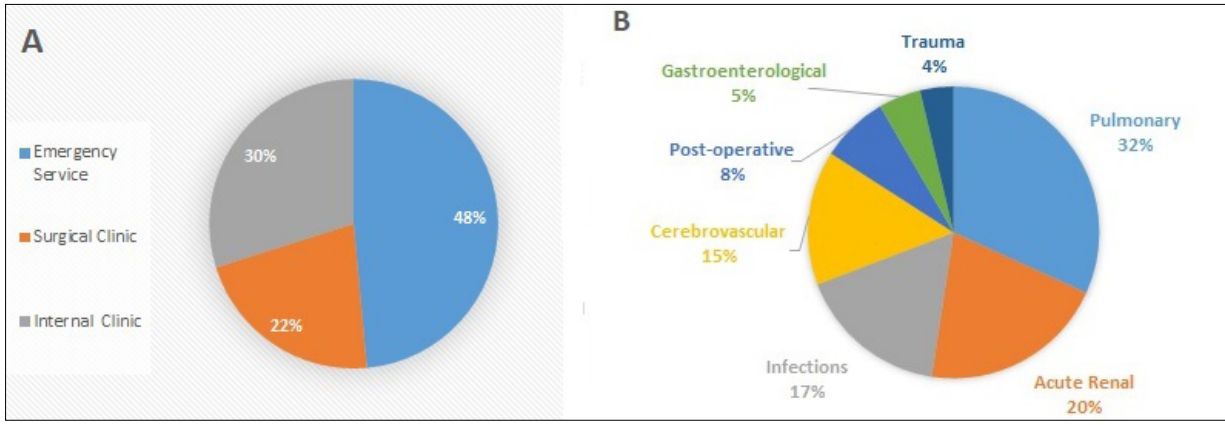

Figure 2. Distribution of patients according to the route of admission **(A)** According to the reasons of admission **(B)**

In the ICU, glucose monitoring and treatment are performed by nurses working in the unit. The nurse-to-patient ratio in these units is 1:2 across all shifts. In patients who require insulin therapy, insulin administration in the ICU is administered intravenously with a perfuser as pure crystalline insulin. In patients whose blood glucose values are stable at the desired levels, blood glucose monitoring is performed at 4-h intervals. Blood glucose monitoring is more frequently performed in patients who are started on steroids, who develop sepsis or septic shock, who are started on vasopressors, whose nutrition is started or whose contents and routes are changed, who are started on renal replacement therapy, or who develop acute liver failure. Values of 60 mg/dL and below were accepted as hypoglycemia. Blood glucose measurement is usually done at the bedside, using capillary blood and a glucometer (GlucoDr SuperSenso). In patients with abnormal values, blood glucose values are compared with the study of the venous blood sample in the hospital central laboratory.

Statistical Analysis

All statistical analyses were performed using the SPSS (Statistical Package for Social Sciences) software, version 21.0 (IBM Corp., Armonk, NY). Quantitative variables expressed as mean±standard deviation, were compared using the One-way ANOVA test. The qualitative variables were expressed in percentages and compared using either the chi-square test or Fisher's exact test. The Pearson's correlation analysis was used to determine the relationship between the glucose regulation results and the variables. A $p<0.05$ was considered statistically significant.

RESULTS

On the study day, 132 patients were hospitalized in the ICU, 107 patients (Covid ICU [C-ICU] n=35 and non-Covid ICU [NC-ICU] n=72) met the criteria for this study and were included in the study (Figure 1).

The mean age of the patients was 60±14.6 years and 47.6% (n=51) were male. 48.6% of the patients were hospitalized from the emergency department, and the most common reason for admission to the ICU was pulmonary causes (32%) (Figure 2). The average number of ICU days of the patients was 9 (4–14) days. 59.8% (n=64) of the patients were receiving invasive mechanical ventilation support, 35.5% (n=38) were receiving inotropic support, and 9.3% (n=10) were receiving CRRT support. Considering their diet, 11.2% were fed orally, 12.1% with percutaneous endoscopic gastrostomy, 43.9% with Nasogastric tube, and 8.4% with total parenteral nutrition (Table 1).

The characteristics of the patients regarding glycemic control on the study day are presented in Table 2. Among them, 29.9% of the patients had a diagnosis of DM, 9.3% were receiving insulin infusion therapy and 12.1% were receiving long-acting insulin therapy. Hyperglycemia was detected in 25.2% of all patients, hypoglycemia in 4.7%, and glycemic dysregulation in 29.9% in total. The mean

Table 1. Demograhic and clinical characteristics of patients (n=107)

Variables	Results
Age, year (mean±SD)	60±14.6
Gender, n (%)	
Male	51 (47.6)
Female	56 (52.4)
LOS, days	9 (4-14)
APACHE II	21.2 ±3.6
SOFA	5.7±1.3
Requirement of ALS, n (%)	
MV	64 (59.8)
Vasoactive support	38 (35.5)
CRRT	10 (9.3)
Nutritional status, n (%)	
Oral	12 (11.2)
PEG	13 (12.1)
NG	47 (43.9)
TPN	9 (8.4)

APACHE II: Acute physiological and chronic health score; ICU: Intensive care unit; LOS: Length of stay in ICU (The day of study); ALS: Advanced life support; NG: Nasogastric; PEG: Percutaneous endoscopic gastrostomy; TPN: Total parenteral nutrition.

Table 2. Glycemic characteristics of patients (n=107)

Variables	Results n (%)
DM	32 (29.9)
Hyperglycemia	27 (25.2)
Hypoglycemia	5 (4.7)
Dysregulation	32 (29.9)
Insulin infusion	10 (9.3)
Long-acting insulin	13 (12.1)
Steroid replacement	24 (22.4)

blood glucose value of the patients was measured as 158 mg/dL. All the patients who developed hypoglycemia were on insulin therapy.

In the ICUs, total of 32 patients (29.9) had dysregulate (hyperglycemic or hypoglycemic) blood glucose levels. 28.6% (n=10) of these patients were in the C-ICU and 30.5% (n=22) of them were in the NC-ICU. There was no significant difference in blood glucose dysregulation between the two groups (p=0.510) (Table 3).

According to the Pearson correlation analysis, a significant correlation was found between the presence of diabetes and dysregulation in patients (p=0.05), and there was no statistically significant correlation between other parameters and dysregulation.

DISCUSSION

In the literature, it was seen that there are many studies and meta-analyses with different results investigating the range of blood glucose levels and the effect of dysregulation on patient outcomes. The first study studying the effect of intensive insulin therapy on morbidity and mortality in critically ill patients was Van den Berghe's study in surgical intensive care patients in 2001. In this study, it was shown that mortality in ICUs decreased in patients who were treated with intensive insulin for strict blood glucose control.[13] As a result of these positive results, many centers started to implement strict glucose control protocols and shared the results with the literature. With the widespread use of this approach, some meta-analyses have shown that strict glucose control leads to the opposite effects.[3,14] Two multicenter, randomized controlled trials, VISEP and GLUCONTROL, were terminated due to frequent hypoglycemia.[15,16] In the same period, the results of the NICE-SUGAR study were shared with the literature. In this multicenter study, blood glucose level was kept between 81–108 mg/dL in the group receiving intensive insulin therapy, and 180 mg/dL and below in the conventional treatment group, and 90-day mortality was higher in the group receiving intensive insulin therapy (27.5% vs. 24.9%; OR: 1.14% 95% CI 1.02–1.28; p=0.02). This study recommended that blood glucose should not be lowered below 110 mg/dL in critically ill patients and should be kept between 140 and 180 mg/dL.[10] In our study, we aimed to keep the blood glucose values of the patients between 140 and 180 mg/dL according to our clinical practice and observed the results in terms of dysregulation. Our results showed that less than half of the patients had blood glucose levels outside the aimed glucose range, and only 29.9% of all patients developed glycemic dysregulation, the majority of which was in the form of hyperglycemia (25.2%). For this reason, the standard insulin protocol we currently use has been redesigned and updated to two different level protocols, the "high insulin protocol" and "low insulin protocol."

It was found that hypoglycemia developed at a rate of 4.7% in our study. All these patients were NC-ICU patients receiving insulin infusion. To avoid the side effects secondary to hypoglycemia, especially in patients receiving insulin infusion, it was thought that more strict blood glucose monitoring and treatment should be considered.

DM is one of the common comorbidities in COVID-19 patients, but there is not yet enough evidence-based data

Table 3. Glycemic characteristics of patients in Covid-ICU and non-Covid ICU

Variables	C-ICU n (%) n=35	NC-ICU n (%) n=72	p-value
Patients with DM (n, %)	12 (34.3)	20 (28.2)	0.334
Patient on insulin infusion therapy (n, %)	5 (14.3)	5 (6.9)	0.290
Patient on steroid replacement therapy	20 (57.1)	4 (5.6)	0.001
Nutritional status of patients			
Oral	3 (8.6)	9 (12.5)	0.402
NG	22 (62.9)	25 (34.7)	0.005
PEG	3 (8.6)	10 (13.9)	0.327
TPN	3 (8.2)	6 (8.3)	0.530
Hypoglycemia	–	5 (6.9%)	–
Hyperglycemia	10 (28.6)	17 (23.6)	0.480
Dysregulation	10 (28.6)	22 (30.5)	0.510

DM: Diabetes mellitus; NG: Nasogastric; PEG: Percutaneous endoscopic gastrostomy; TPN: Total parenteral nutrition.

for the management of COVID-19 in people with diabetes.[17] The diabetes rate has been reported as 7.4% in COVID-19 patients, and adverse outcomes are 3.1 times more common in diabetic patients compared to non-diabetic individuals.[18] Viral infections can exacerbate diabetes and cause fluctuations in blood glucose in diabetic patients, which adversely affects their prognosis.[19] During glucose management in diabetic patients with COVID-19, the occurrence of hypoglycemia should be minimized. In our study, there was no difference between COVID and NC-ICUs in terms of blood glucose dysregulation. In fact, no hypoglycemia was observed in the C-ICU due to the more frequent use of steroids, and dysregulation manifested itself as hyperglycemia. This situation was attributed to the high rate of steroid treatment in patients.

In our study, we found that blood glucose fluctuates in ICUs, and it is not easy to maintain glycemic control at targeted levels in diabetic or non-diabetic cases. When we looked at the mean daily blood glucose value of the patients with fluctuations, we found that the result remained within the recommended target values (158 mg/dL).

Conclusion

It was observed that a blood glucose level of 140–180 mg/dL increased the susceptibility to hyperglycemia, but less hypoglycemia developed. ICUs should create, use, and update their own blood glucose and insulin protocol, which will reach the target without causing serious hypoglycemia. This approach ensures a certain standard for each patient and improves outcomes.

Limitations

This study has some limitations it is a single-center, point prevalence study. So, its reliability and generalizability are quite low. A glucometer was used for blood glucose measurement. This method has the least reliability in blood glucose measurement. However, it was preferred for reasons such as practicality, immediate results, and not requiring large amounts of blood.

Ethics Committee Approval

This study approved by the Kartal Dr.Lutfi Kirdar City Hospital Clinical Research Ethics Committee (Date: 28.01.2022, Decision No: 2022/514/218/32).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: Y.B.; Design: K.T.S.; Supervision: K.T.S.; Fundings: Y.B.; Materials: Y.Bu., Y.B.; Data: Y.B., Y.Bu.; Analysis: F.C., Y.B.; Literature search: F.C., Y.B.; Writing: Y.B.; Critical revision: Y.B., K.T.S.

Conflict of Interest

None declared.

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Yoğun Bakım Ünitesinde Etkin Glisemik Kontrol Sağlayabiliyor muyuz? Nokta Prevalans Çalışması

Amaç: Kan şekeri disregülasyonu, kritik hastaların mortalite ve morbiditesi ile bağımsız ilişkilidir. Ancak yoğun bakım ünitelerinde diyabetik ve non-diyabetik hastalarda kan glikoz düzeyinin hedeflenen seviyelerde tutulması güçtür. Üçüncü basamak yoğun bakım ünitesinde (YBÜ) yatarak tedavi görmekte olan hastalarda kan şekeri regülasyonunu değerlendirmek amacıyla nokta prevelans çalışması planlandı. Araştırmaya başlamadan önce etik kurul onayı alındı.

Gereç ve Yöntem: Hastaların demografik verileri, başvuru anındaki özellikleri, yoğun bakım takip ve tedavileri, uygulanan beslenme şekilleri ve glisemik kontrolle ile ilgili parametreler standart veri forumuna kaydedilerek değerlendirildi.

Bulgular: Çalışma günü, 35 COVID (C-YBÜ) ve 72 Non–COVID yoğun bakım ünitesinde (NC-YBÜ) yatmakta olan toplam 107 hasta çalışmaya dahil edildi. Hastaların 47.6%'sı erkek idi ve %29.9'unda diyabet mellitus (DM) tanısı mevcuttu. İstatistik sonuçlarına bakıldığında; Hastaların ortalama kan şekeri değeri 158 mg/dL olarak ölçüldü, tüm hastaların %29.9'unda glisemik disregülasyon (%4.7'sinde hipoglisemi, %25.2'sinde hiperglisemi) tespit edildi. Yoğun bakımlara göre bakıldığında C-YBÜ'de %28.6 (n=10) hastanın kan şekerinin regüle olmadığı, NC-YBÜ'de %30.5 (n=22) hastanın kan şekerinin regüle olmadığı tespit edildi. İki grup arasında kan şekeri regülasyonu açısından oranlar benzerdi (p=0.510). DM varlığı ile kan şekerinin disregüle seyretmesi arasında istatistiksel olarak anlamlı korelasyon tespit edildi (p=0.05).

Sonuç: Günümüzde belli glikoz hedefinin tüm hastalar için her zaman optimal olmayabileceği ve glikoz kontrolünün bireyselleştirilmesi fikri tartışılmaktadır. Rutin işleyişte hastaları hipoglisemi ve hiperglisemiye sokmadan, her kliniğin kendi kan şekeri algoritmasını oluşturup, sıkı takip ile iyi bir metabolik kontrol sağlaması gerektiği kanaatindeyiz.

Anahtar Sözcükler: Glisemik kontrol; hipoglisemi; hiperglisemi; yoğun bakım ünitesi.