ORIGINAL ARTICLE

Prognostic Value of Serum Glucose Level in Critically Ill Septic Patients on Admission to Pediatric Intensive Care Unit

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Abstract

Background: Sepsis is one of the major causes of admission to the pediatric intensive care unit (PICU), as well as a primary cause of poor outcomes. Glycemic variation may occur because of sepsis resulting in either hypoglycemia or hyperglycemia. Measuring the random blood glucose (RBG) level of patients presenting with sepsis in PICU is an easy way to assess their prognosis.

Objectives: A prospective study was done from February 2023 to June 2023 to evaluate the relation between the outcome of pediatric septic patients and blood glucose level upon PICU admission.

Patients and methods: One hundred three children diagnosed with sepsis underwent clinical assessment upon admission to the PICU and initial labs including blood glucose levels were done. Pediatric Sequential Organ Failure Assessment (pSOFA) was calculated for every patient. The outcome of sepsis including length of stay, review of body systems, and mortality was documented.

Results: Hypoglycemic patients had the highest percentage of non-survivors (20.4%). They had a higher pSOFA score with a median of 11 (interquartile range—IQR 7–15), shorter PICU stay with a median of 2 (IQR 1–6) days, lower RBG with a median of 95 (45–120), a higher percentage of ventilation (55.1%), and a higher percentage of inotropic support (87.8%) with statistical significance with *p*-value (< 0.001, < 0.001, 0.001, < 0.001, 0.002), respectively.

Conclusion: Critically ill patients with abnormal random blood sugar (RBS) had a higher possibility of non-survival particularly those with hypoglycemia. Accordingly, RBS measurement is a rapid and cheap method that could be used in any emergency and as an early indicator to detect outcome.

Keywords: Children, Hypoglycemia, Mortality, Sepsis.

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Highlights

The abnormality in glucose hemostasis is observed in septic patients in the pediatric intensive care unit (PICU). We have found that low random blood sugar is associated with poor outcome regarding the survival status and need for mechanical ventilation and/or inotropic support.

Introduction

The burden of sepsis in children is estimated to be 1.2 million cases yearly, with the death of 1–5% of septic patients and 9–20% of severely septic patients.[1] Sepsis is due to the disparity of patients' reactions to infection and subsequently affecting multiple organs.[2] Therefore, prompt management of septic patients on admission is crucial.[3]

During sepsis, glucose homeostasis is affected and can result in a wide range of blood glucose levels.[4–6] Several hormones play a vital role in maintaining blood glucose levels such as thyroid hormone, cortisol, glucagon, growth hormone, and adrenaline.[7] Sepsis commonly results in hyperglycemia[7–9] because of increased insulin resistance while hypoglycemia is reported infrequently.[10] However, hypoglycemia may be caused by several mechanisms such as deficiency of cortisol and adrenaline hormone, failure of liver gluconeogenesis leading to alteration of glucose metabolism, and the possibility of rise of glucose consumption in peripheral tissues.[11] Hypoglycemia can result subsequently as a part of the disease process. On the other hand, hypoglycemia can lead to impairment of autonomic function, cytokine release, white cell activation, and fatal cardiac arrhythmia.[12] Our study aimed to determine the relation between the outcome of patients presenting with sepsis and blood glucose level initially at PICU admission.

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Conflict of interest: None

Patients and Methods

This prospective study was performed in the PICU, between February and June 2023. The study included 103 septic patients with age ranging from 1 month to 14 years. Sepsis was diagnosed if children presented with systemic inflammatory response syndrome (any two of the following): (1) Core temperature >38°C or <36°C. (2) Tachycardia or bradycardia not due to an external stimulus. (3) Tachypnea not caused by neuromuscular disease. (4) Leucocyte count abnormal for age or over 10% immature neutrophils.[13]

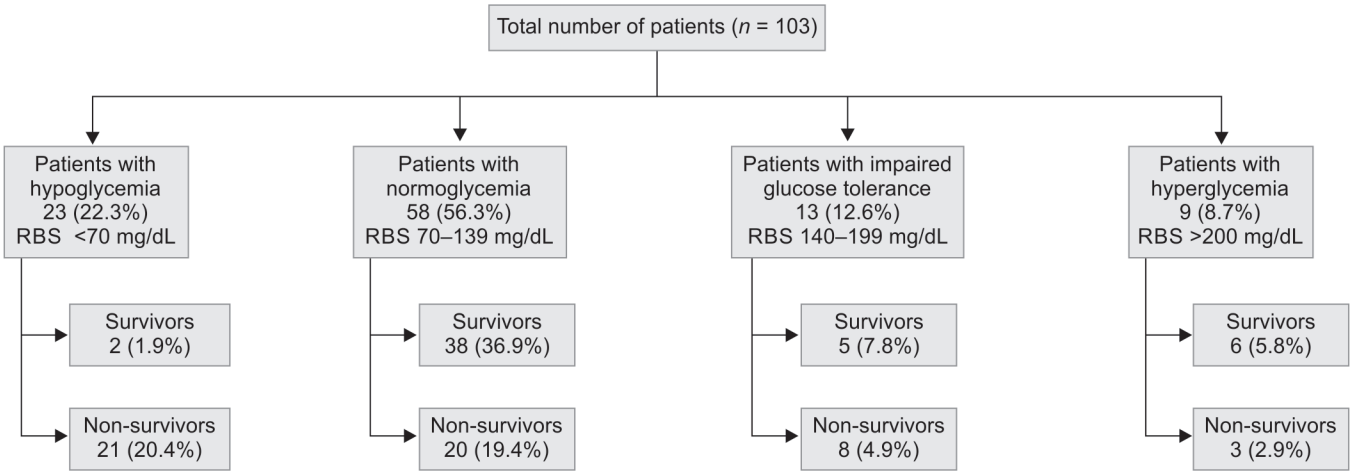


Fig. 1: Flowchart of patients included in this study

Patients were excluded if they were admitted for reasons other than sepsis, had any cause of hypoglycemia, or had diabetes. Informed consent was acquired from all enrolled patients. Our study protocol was approved by the Research Ethics Committee (N-34-2023).

Once the patients were admitted, a comprehensive medical history and examination were performed. Initial laboratory tests were performed including blood glucose level, complete blood count with differential, C-reactive protein, arterial blood gases, liver function tests, kidney function tests, coagulation profile, and cultures. The Pediatric Sequential Organ Failure Assessment (pSOFA) score was calculated for all patients. The outcome of sepsis including review of body systems, PICU length of stay, residual morbidities at PICU discharge, and mortality were recorded.

Statistical Analysis

Statistical package for the Social Sciences version 28 (IBM Corp., Armonk, NY, United States) was used for coding and data entry. Quantitative data were expressed using median and interquartile range (IQR) and categorical data using frequency (count) and relative frequency (percentage). The non-parametric Kruskal–Wallis and Mann–Whitney tests were used for comparing quantitative variables.[14] The Chi-square test was utilized for comparing categorical data. But when the expected frequency was less than 5, the Exact test was used.[15] The Spearman correlation coefficient was used to correlate between quantitative variables.[16] Statistical significance was considered when *p*-values were less than 0.05.

Results

A total of 103 patients were included in this study and divided them into four groups: patients with hypoglycemia (22.3%) with RBS <70 mg/dL; patients with normoglycemia (56.3%) with RBS 70–139 mg/dL; patients with impaired glucose tolerance (12.6%) with RBS 140–199 mg/dL; and patients with hyperglycemia (8.7%) with RBS >200 mg/dL. They were further divided into 54 survivors (52.4%) and 49 non-survivors (47.6%). Patients with hypoglycemia had the highest percentage of non-survivors (20.4%) while patients with normal blood glucose had the highest percentage of survivors (36.9%) as shown in Figure 1.

The characteristics and laboratory investigations of the patients are presented in Table 1. The median age was 1 year (IQR 0.04–4), the median pSOFA score was 8 (IQR 3–12), the median random blood glucose (RBG) was 110 (IQR 80–131) mg/dL, and the PICU length was 4 (IQR 4–9) days.

Table 1: Baseline characteristics and laboratory investigations

	Median	*Interquartile range*
Age (years)	1	0.4–4
Systolic blood pressure (mg/dL)	85	75–100
Diastolic blood pressure (mg/dL)	50	40–60
Temperature (°C)	38.5	38–39
Heart rate (per min)	140	125–160
Respiratory rate (per min)	35.5	33–45
Capillary perfusion (sec)	3	3–4
Glasgow coma scale	13	10–15
Pediatric sequential organ failure assessment score	8	3–12
Hemoglobin (g/dL)	9.7	8.6–10.8
Total lymphocytic count (per µL of blood)	17	8–20.4
Staff/Segmented	0.21	0.06–0.25
Platelets (per µL of blood)	302	92–433
CRP (mg/dL)	48	6–96
ALT (U/L)	42	20.5–144
AST (U/L)	75	35–191
Urea (mg/dL)	36.5	20–92
Creatinine (mg/dL)	0.7	0.5–1.2
Sodium (mmol/L)	138	135–145.5
Potassium (mmol/L)	4.3	3.55–5
Random blood glucose (mg/dL)	110	80–131
PICU length of stay (days)	4	2–9

Regarding patients' outcome, non-survivors showed higher pSOFA score with a median score of 11 (IQR 7–15), shorter PICU stay with the median being 2 (IQR 1–6) days, lower RBS with a median of 95 (45–120), a higher percentage of ventilation (55.1%), and a higher percentage of inotropic support (87.8%) with statistical significance. However, there was no statistical difference between

Table 2: Comparison between survivors and non-survivors

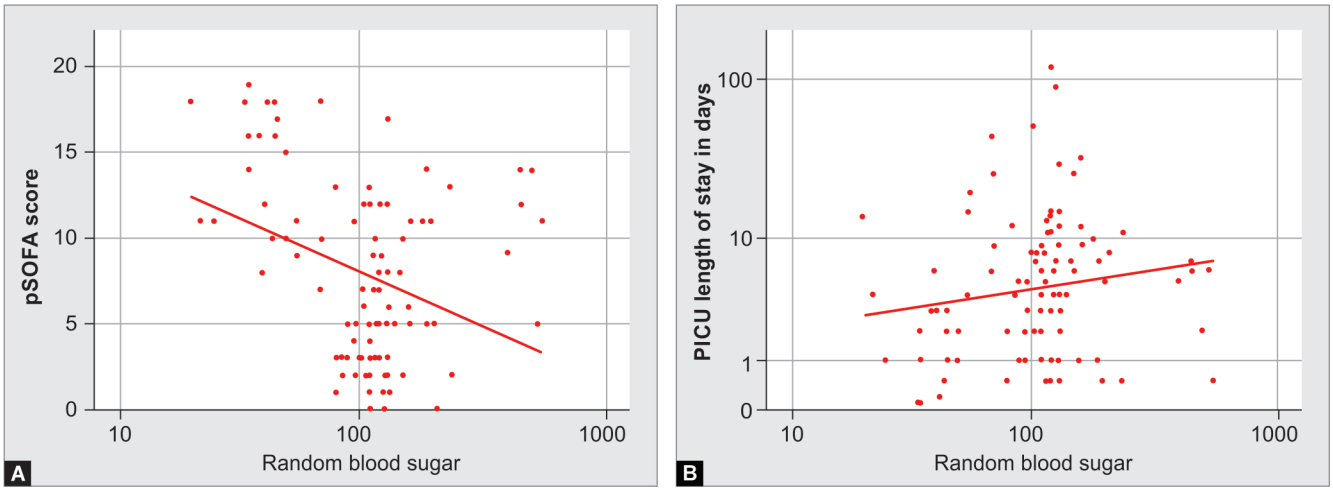
Variables	*All patients (n = 103)*	*Survivors (n = 54)*	*Non-survivors (n = 49)*	*p-value*
Male	51 (49.5%)	26 (48.1%)	25 (51.0%)	0.771
Female	52 (50.5%)	28 (51.9%)	24 (49.0%)	
± System affection				
No	1 (1.0%)	1 (1.9%)	0 (0%)	1
Yes	102 (99.0%)	53 (98.1%)	49 (100.0%)	
pSOFA	8 (3–12)	4.5 (2–9)	11 (7–15)	<0.001
PICU stay	4 (2–9)	6 (3–9)	2 (1–6)	<0.001
RBS (numbers)	110 (80–131)	120 (97–139)	95 (45–120)	0.001
Mechanical ventilator				
Yes	36 (35.0%)	9 (16.7%)	27 (55.1%)	<0.001
No	67 (65.0%)	45 (83.3%)	22 (44.9%)	
Inotropic support				
Yes	76 (73.8)	33 (61.1%)	43 (87.8%)	0.002
No	27 (26.2	21 (38.9%)	6 (12.2%)	

Data shown as number (%) or median (interquartile range)

Table 3: Correlation between RBS and age of the patients, pSOFA and PICU length of stay in days

	RBS				
	Hypoglycemia	*Normal*	*Impaired*	*Hyperglycemia*	*p-value*
Age (years)	0.50 (0.30–3.00)	1.00 (0.50–5.00)	1.00 (0.60–1.30)	0.70 (0.20–2.00)	0.343
pSOFA score	15.00 (10.00–18.00)	5.00 (2.00–8.00)	6.00 (5.00–11.00)	11.00 (5.00–13.00)	<0.001
PICU length of stay (days)	2.00 (1.00–6.00)	4.00 (2.00–9.00)	7.00 (4.00–10.00)	6.00 (2.00–7.00)	0.164

Data shown as median and interquartile range



Figs 2A and B: Correlation between random blood glucose and Pediatric Sequential Organ Failure Assessment score and between random blood glucose and pediatric intensive care unit length of stay in days

survivors and non-survivors regarding gender or the presence of system affection as shown in Table 2.

In our study, we found a positive correlation of statistical significance between RBS groups and pSOFA score with *p*-value <0.001 while the age of the patients and the PICU length of stay showed no statistical significance as demonstrated in Table 3.

Figure 2A shows an inverse relation between RBS and pSOFA score with a correlation coefficient of −0.295 and *p*-value of 0.002, and Figure 2B shows a positive correlation between RBS and PICU length of stay in days with a correlation coefficient of 0.228 and *p*-value of 0.020.

The non-survivors were 49 (47.6%) patients; 21 (91.3%) of them belonged to the hypoglycemic group with a statistical significance of <0.001. On reviewing the body systems, the central nervous system and hematological or metabolic were the main causes of mortality where 17 (73.9%) and 10 (43.5%) patients, respectively, belonged to the hypoglycemic group with a statistical significance of < 0.001.

Discussion

Sepsis is a significant cause of morbidity and mortality in children. Glucose homeostasis varies among children with septic shock.[17] Therefore, we aimed to detect the relation between critically ill septic patients and their initial RBG.

In our study, we found that patients with hypoglycemia were at higher risk of mortality, which is similar to the findings of many other studies.[12,18–24]

However, these study findings were contradicted by the following studies: Blesa Malpica et al.,[25] Freire et al.,[26] and Larrondo Muguercia et al.[27] They showed that the RBG level of septic patients on the first day of admission to the PICU was not an indicator of mortality. However, they found a direct relation between hyperglycemia and patients' morbidity. Consequently, they recommended blood glucose monitoring to denote metabolic instability.

This study found that the mortality rate in hypoglycemic patients was 20.4% compared with 2.9% in hyperglycemic patients, which was in concordance with a study by Toro-Polo et al.[28] However, this was contrasting to the findings of other studies, which showed that patients with higher RBG had higher mortality rate.[29–32] Therefore, we concluded that glycemic variation leads to mortality, as observed in this study. We also found that both hypoglycemia and hyperglycemia have the potential risk for mortality, but the hypoglycemic group is at higher risk.

This study demonstrated that non-survivors had shorter PICU stay, with a median of 2 (IQR 1–6) days, which may be the cause of their shorter stay and subsequent mortality. On the other hand, another study by de Farias et al.[17] revealed that PICU stay did not significantly affect the outcome, with a *p*-value of 0.08.

Moreover, this study has demonstrated that 55.1% of the non-surviving patients were ventilated with a significant correlation with mortality with *p* value of less than 0.001. This agrees with the reports of Tirkey and Verma[33] and Toro-Polo et al.,[28] who reported that the non-survivors had a higher percentage of ventilation (85%) with a *p*-value of less than 0.0001. While a study carried out by Bagshaw et al.[19] demonstrated that patients with glucose variability were more likely to be ventilated.

Also, non-survivors had a higher percentage of inotropic support (87.8%) with a statistical significance, which is in accordance with the following studies: Tirkey and Verma[33] and de Farias et al.[17] However, we found no statistical difference between living and deceased patients regarding gender or the presence of any system affection.

Additionally, this study showed an inverse relation between RBG and pSOFA score where the hypoglycemic group had a higher pSOFA score, and, to our knowledge, no study has shown this relation.

However, this study demonstrated a positive correlation between RBS and PICU length of stay, which is in contrast with Bagshaw et al.'s study,[19] which showed that initial hypoglycemia was associated with a longer PICU stay.

Limitations of the Study

This study was conducted in a single center over a period of 6 months duration using the initial RBG and other variables such as glucocorticoid and nutrition were not considered. A larger study with a longer duration and multiple random blood glucose measurements is recommended.

Conclusion

Abnormal RBG level can lead to mortality in critically ill patients. Hypoglycemic patients have a higher probability of mortality, higher pSOFA score, lower RBG, and a higher probability of being ventilated and in need of inotropic support. Therefore, RBS in PICU should be considered as a guide for prognosis and should be observed and corrected. In view of the shortage of supplies in many developing countries and the sociodemographic and civilization variations of the population, it is crucial to utilize an economical method that is readily available to predict patients at potential risks.

Clinical Significance

Random blood sugar measurement is a rapid and cheap method that could be used as an early indicator to detect outcome in critically ill septic patients.

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