Original Article

Correlation between Stable Hyperglycemia and Mortality in Children Admitted to the Pediatric Intensive Care Unit of Imam Hossein Hospital

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Abstract

Background: Stress-induced hyperglycemia is an important issue among pediatrics admitted in the pediatric intensive care unit (PICU). Former studies have declared that hyperglycemia has a high prevalence rate and could increase the risks of mortality among pediatrics. Here, we aimed to investigate the prevalence rate of hyperglycemia and its effects on mortality among pediatrics in the PICU of the hospital. **Materials and Methods:** This cross-sectional study was performed in 2018–2019 on 88 patients admitted in PICU. Data regarding blood sugar (BS) and other clinical and laboratory parameters were collected. Hyperglycemia was accounted for as BS of >126 mg/dl. Hyperglycemia was divided into: mild (126 <BS <150), moderate (150 <BS <200) and severe (BS >200). The pediatric risk of mortality (PRISM) score was also calculated for each patient during the first 24 h. **Results:** Thirty patients (34.1%) had persistent hyperglycemia and 58 patients (65.9%) had normal glycemic indexes. Eleven patients (12.5%) had mild, 9 patients (10.2%) had moderate, and 10 patients (11.4%) had severe hyperglycemia. The prevalence of mortality was 5.7% among hyperglycemic patients and 6.8% among normal glycemic pediatrics. There were no statistically significant differences regarding mortality rate (P = 0.499). The mean PRISM score for normal glycemic patients was 7.03 ± 5.18 and for patients with hyperglycemia was 7.36 ± 6.37. **Conclusion:** Hyperglycemia has no significant effects on mortality and PRISM score of pediatrics in PICU, despite of the previous studies. The frequency of hyperglycemia was also 5.7% among the patients admitted in PICU.

Keywords: *Hyperglycemia, mortality, intensive care units, pediatric*

Introduction

The pediatric intensive care unit (PICU) is one of the most important units in every pediatric hospital. Studies indicate that each year, more than 10,000 children are admitted to PICU due to different causes.[1] Stress-induced hyperglycemia is one of the critical complications with which patients in PICU might deal with.[2,3] Previous studies show that 4%–12% of hospitalized non-diabetic patients could develop stress-induced hyperglycemia, which might be associated with increased risks of mortality and morbidities.[4] The main mechanism of this issue is that hyperglycemia is thought to increase inflammatory mediators and induce oxidative stress, which results in deterioration of the patient's clinical conditions.[5-7]

Stress-induced hyperglycemia increases the activity of the sympathomimetic system and induces the release of both counterregulatory hormones and pre-inflammatory cytokines.[8] Increased peripheral resistance to insulin, relative insufficiency of insulin, disrupted glucose metabolism, and external factors, including drugs such as catecholamine, corticosteroids, and exogenous dextrose administrations, are also known to be the main etiologies of stress-induced hyperglycemia.[9] Studies also indicated that stress is a triggering factor for counter-regulatory hormones, including glucagon, epinephrine, cortisol, and growth hormone, which can be accounted for as other etiologies for hyperglycemia during stress.[10] Bleeding, hypoxia, and sepsis cause the highest levels of epinephrine and norepinephrine.[11,12]

There have been some studies on adults, which indicated that the prevalence of hyperglycemia is related to higher mortality rates. Some other studies on pediatrics have

How to cite this article: Reisi M, Keivanfar M, Mostofizadeh N, Madihi Y, Esmaeilian Y, Hashemi E. Correlation between stable hyperglycemia and mortality in children admitted to the pediatric intensive care unit of Imam Hossein Hospital. Adv Biomed Res 2021;10:2.

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Received: 04 February 2020
Revised: 07 April 2020
Accepted: 22 April 2020
Published: 27 January 2021

Access this article online

Website: www.advbiores.net

DOI: 10.4103/abr.abr_31_20

Quick Response Code:

also mentioned the same results. It has been also mentioned that the prevalence of hyperglycemia is lower in pediatrics because of the lower prevalence of diabetes mellitus.[13] Other studies believe that the duration of hyperglycemia and changes in glycemic indexes are related to mortality rates in patients with critical conditions.[14] They have reported that hyperglycemia is a negative predicting factor in children with severe head trauma and injuries and multiple organ trauma.[15] Studies on adults indicated that stress-induced hyperglycemia has different negative effects on multiple organs, including cardiovascular system (acute myocardial infarction, cardiogenic shock, and arrhythmia), neuromuscular system (polyneuropathy), and immune system (suppressed immune system and hospital-induce infections).[10,16] It may also cause stroke and delayed wound healing.[17,18]

On the other hand, some evaluating systems have been developed to evaluate the general condition of pediatric patients admitted to PICU. Pediatric risk of mortality (PRISM) is one of these systems which was developed by Pollack *et al.* in 1998.[19] This system evaluates the clinical and laboratory characteristics of patients and can give a score and assess the condition of patients. There have been some previous studies performed to evaluate the effects of hyperglycemia in pediatrics. Here for the first tie, we aimed to perform a study on children admitted in the PICU of Imam Hossein hospital in Isfahan to assess the effects of hyperglycemia on mortalities of patients and their PRISM score.

Materials and Methods

This is a cross-sectional study performed in 2018–2019 on patients admitted in the PICU of Imam Hossein hospital in Isfahan. The current study was approved ethically by the ethical committee of Isfahan University of Medical Sciences. In this study, all patients with the age of 1 month to 16 years who have been admitted to the PICU were included in the study. Written informed consent was signed by parents. These patients were excluded from this study: Patients who were discharged from PICU to any other wards within the first 24 h, patients who expired during the first 24 h, patients who had been admitted in another PICU before the current admission in patients with a history of diabetes mellitus, patients who were under long term treatments with corticosteroids, beta-agonists, and other drugs which can induce hyperglycemia, patients who had previously received intravenous glucose with a glucose infusion rate more than 6 mg/kg/min.

Based on our inclusion and exclusion criteria, 88 patients were entered into this study. Primary data regarding the age, sex, medical history, primary diagnosis, and vital signs were collected. PRISM score was calculated for each patient based on the clinical and laboratory data within the first 24 h. Systolic blood pressure, heart rate, body temperature, pupil reflex, state of consciousness, blood gas, blood urea nitrogen, serum creatinine, blood sugar (BS), white blood cells, and platelets were measured in the first 24 h for each patient and collected to PRISM calculations.

BS of patients was measured by the admission time using Zyklusmed TD-4267 glucometer. Hyperglycemia was accounted for as BS of >126 mg/dl. BS between 126–150 mg/dl was accounted for as mild hyperglycemia. Moderate hyperglycemia was considered as BS between 150 and 200 mg/dl, and severe hyperglycemia was BS of >200 mg/dl.[20] Patients were also followed up until discharge or transmission to another ward or expiration.

Results

Here in this study, 88 children admitted in the PICU of Imam Hossein Hospital in 2018–2019 were evaluated. Our study population consisted of 44 males and 44 females. Thirty patients (34.1%) had persistent hyperglycemia[20] and 58 patients (65.9%) had normal glycemic indexes. Further analysis showed that 17 patients (19.3%) in the hyperglycemic group were males and 13 patients (14.8%) were females. Age distribution of patients indicated that thirty patients (34.1%) were between 1 and 6 months. There was also no significant difference between the two groups regarding the sex and age ($P > 0.05$). Distribution of patients regarding their age and cause of admitting in PICU is summarized in Tables 1 and 2. Pneumonia and neurologic diseases were the most common causes of PICU hospitalization. Our results also indicate a 12.5% mortality rate (11 patients).

Data analysis regarding to hyperglycemia indicated that 11 patients (12.5%) had mild hyperglycemia

Table 1: Age distribution of patients

Age group	Frequency (%)	Cumulative percent
1-6 months	30 (34.1)	34.1
6-12 months	13 (14.8)	48.9
12-24 months	14 (15.9)	64.8
2-6 years	18 (20.5)	85.2
6-12 years	11 (12.5)	97.7
>12 years	2 (2.3)	100.0
Total	88 (100.0)	

Table 2: Cause of the pediatric intensive care unit hospitalization

Cause	Frequency (%)	Cumulative percent
ARDS	4 (4.5)	4.5
Pneumonia	34 (38.6)	43.2
Sepsis	7 (8.0)	51.1
Postoperation	9 (10.2)	61.4
Neurologic	27 (30.7)	92.0
CHD	4 (4.5)	96.6
Renal disease	3 (3.4)	100.0
Total	88 (100.0)	

ARDS: Acute respiratory distress syndrome, CHD: Coronary heart disease

(126 <BS <150), 9 patients (10.2%) had moderate hyperglycemia (151 <BS <200), and 10 patients (11.4%) had severe hyperglycemia (BS > 200). Calculations for PRISM score indicated that the mean PRISM score for normal glycemic patients was 7.03 ± 5.18 and for patients with hyperglycemia was 7.36 ± 6.37. We also showed that there was no significant difference between the two groups regarding PRISM score ($P > 0.05$). The mean PRISM score based on levels of hyperglycemia is summarized in Table 3.

Analysis of mortality in each group showed that 5 patients (5.7%) with persistent hyperglycemia were expired with similar etiology while on the other hand, 6 other expired patients (6.8%) were in the normal glycemic group. There was also no significant difference between the two groups regarding mortality rate ($P = 0.499$).

Discussion

Here in this study, we indicated that there is no significant difference between patients with stress-induced hyperglycemia and patients with normal glycemic indexes regarding PRISM score and mortality rate with similar etiology. We also showed that the frequency of hyperglycemia is 5.7% among patients admitted to the PICU. We believe that the absence of a significant difference between mortalities among pediatrics might be due to their clinical conditions and mortality etiologies. There have been many previous studies performed on this issue, most of which declare that hyperglycemia increases the risks of mortality and duration of hospitalization. Klein and others had a study on 1550 pediatrics in 2008 in the United States of America. They evaluated prevalence and complications of hyperglycemia in PICU based on PRISM scores and reported that the prevalence is 14.3% among children. They concluded that hyperglycemia in the first 24 h of PICU admission is not independently associated with increased mechanical ventilation time, length of stay, or mortality.[21] These results are somehow in line with this study. However, we reported that the prevalence rate for hyperglycemia is 34.1%, which is higher than what they reported, but we also reported no significant difference between mortality rates among pediatrics with hyperglycemia and patients with normal BS. In a study by Kupper *et al*. in 2005, they evaluated 1094 pediatrics who were admitted to PICU and concluded that the prevalence of hyperglycemia is 18.6%, and the mortality rate is 15.2% among patients.[13] These results are not in line with the results of our study. We reported a 34.1% prevalence rate for hyperglycemia and 5.7% mortality rate among them. These differences could be due to different variables, including study populations, mortality causes, and also clinical conditions of patients.

Srinivasan and others also declared that the prevalence of hyperglycemia is high among critically ill pediatrics. They had a study on 152 patients who received vasoactive infusions or mechanical ventilation and reported 86% prevalence rate for hyperglycemia.[22] These results are also not in line with our study, which could be due to different etiologies of PICU admission or mortality. Furthermore, in another study in 2009 by Hirshberg and others, they indicated that 56.1% of critically ill patients experienced hyperglycemia, which was also related to increased mortality rate. They suggest that actions must be performed to control blood glucose, which might lead to improved outcomes in critically ill children.[23] These studies have also reported different results compared to this study. Despite what most of the former studies believe, we found no significant difference between mortality rates and PRISM scores of children admitted in PICU, which cast doubt on what is previously reported. These paradoxical results might be due to differences in both the study population and the basic clinical situations of patients.

The high incidence of hyperglycemia and its association with mortality is also reported by Patki and Chougule. They had a study on 101 pediatrics admitted in PICU and reported a 69.3% prevalence rate for hyperglycemia.[8] They also calculated the PRISM score for both hyperglycemic and nonhyperglycemic patients and showed that there was no significant difference between the two groups regarding to PRISM score. In another study by Abid Khan and others, they also reported a poor outcome for patients with hyperglycemia and a higher mortality rate among them.[24] These studies are also not completely in line with our results. As discussed above, this might be due to study and patient's differences, but we also suggest that hyperglycemia in patients admitted in PICU might not be as frightening as previously thought. We observed no significant difference in mortality rate and PRISM score among two groups of patients. The early management of hyperglycemia could also be critical for better results. Taken together, we suggest more studies on larger populations should be performed to clarify this issue.

Conclusion

We indicated that hyperglycemia has no significant effects on mortality and PRISM score of pediatrics in PICU,

Table 3: Pediatric risk of mortality score based on levels of hyperglycemia

Level of hyperglycemia	Number of patients	Mean PRISM score	SD	95% CI for mean	
				Lower bound	Upper bound
Mild	11	7.2727	5.51527	3.5675	10.9779
Moderate	9	6.3333	5.83095	1.8513	10.8154
Sever	10	8.4000	8.03050	2.6553	14.1447

PRISM: Pediatric risk of mortality, SD: Standard deviation, CI: Confidence interval

despite what most of the previous studies declared. We also showed the frequency of hyperglycemia is 5.7% among patients admitted in PICU.

Financial support and sponsorship

This study was granted by Isfahan University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

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