IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

Open Access
Original Article

Impact of Hyperglycemia Duration on Mortality and Ventilator Dependence in Neonatal Intensive Care Unit

Vahideh Banna Zadeh[1], Gholamreza Khademi[2], Forugh Rakhshanizadeh[3], Bahareh Imani[3], Nooshin Abdollahpour[4], Majid Sezavar[3]*

1. Department of Nutrition, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Neonatal Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad Iran
3. Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
4. Department of Biology, Faculty of Sciences, Young Researchers and Elite Club, Islamic Azad University, Mashhad Branch, Mashhad, Iran

ABSTRACT

***Background*:** Hyperglycemia is an independent risk factor for mortality in neonatal intensive care units (NICU). Herein, we aimed to investigate the relationship of hyperglycemia duration with mortality and ventilator dependence in infants admitted to NICU.

***Methods*:** In this original retrospective study, data was collected between October 2015 and December 2015 from NICU of Dr. Sheikh Children's Hospital in Mashhad, Iran. The studied samples (n=112) were 0-3 month old infants who were admitted to this hospital and were followed up until discharge. Information related to blood sugar was collected based on the samples routinely taken using a glucometer every six hours and were recorded in each patient's blood sugar chart.

***Results*:** Of the subjects, 46.4% (n=52) had blood sugar ≥ 126 mg/dl and 53.6% (n=60) had blood sugar ≤ 40-125 mg/dl. Mann-Whitney and logistic regression tests were used to analyze the data. In this study, we controlled the effect of confounding variables; a significant association was observed between mortality and duration of hyperglycemia (P=0.002). In addition, a significant association was observed between duration of hyperglycemia and ventilator dependence (P=0.02).

Conclusion: Our study showed that the duration of hyperglycemia is positively associated with mortality and ventilator dependence in infants admitted to NICU.

Keywords: Duration of hyperglycemia, Hyperglycemia, Infants, Length of stay, Mortality, Neonatal intensive care unit, Ventilation

Introduction

Hyperglycemia is a normal response to stress in critically ill children providing the glucose dependent organs, such as the brain and blood cells, with energy (1). Hyperglycemia, a frequent event in critically ill children, is associated with poor outcomes, including increased length of stay (LOS), high infection rates, elongated duration of mechanical ventilation, and high mortality rate; proper glycemic control may improve survival (2, 3). Some causes, such as peripheral insulin resistance, relative insulin deficiency, impaired sugar metabolism, and medications such as catecholamine, gluco-corticoids, and exogenous dextrose may also lead to hyperglycemia (4). Endogenous elevation of glucose production through gluconeogenesis and glycogenolysis, as a result of increased regulatory hormones (including cortisol, catecholamines, glucagon, and growth hormone), together with a reduction in insulin-stimulated uptake of glucose by peripheral tissues can also bring about hyperglycemia (2, 5).

Incidence of hyperglycemia in critically ill non-diabetic children is high (4). Mechanical ventilation and inotropic support, length of pediatric ICU (PICU) stay, and mortality rate are significantly higher in hyperglycemic children than in non-hyperglycemic ones (4). It has been found that high

* *Corresponding author:* Majid Sezavar, Pediatric Intensive Care, Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Tel: +98 513 7275580; Email: Sezavarm871@mums.ac.ir

Please cite this paper as:
Banna Zadeh V, Khademi Gh, Rakhshanizadeh F, Imani B, Abdollahpour N, Sezavar M. Impact of Hyperglycemia Duration on Mortality and Ventilator Dependence in Neonatal Intensive Care Unit. Iranian Journal of Neonatology. 2017 Jun: 8(2). DOI: 10.22038/ijn.2017.21036.1238

blood glucose peak and long duration of hyperglycemia are independently associated with mortality (6). Additionally, in non-diabetic children admitted to PICU a maximum blood glucose level higher than 150 mg/dl within 24 hours together with a peak blood glucose concentration higher than 120 mg/dl within 10 days of admission were correlated with in-hospital mortality (5). Hyperglycemia at 24 hours (present in 54% of the subjects) is associated with 3.5 times higher mortality rate. Furthermore, longer duration of hyperglycemia and a higher peak blood glucose value during PICU stay are linked with adverse outcomes (5).

Recent studies indicated that hyperglycemia is a significant concern among physicians caring for critically ill children and that glycemic management is routinely performed to improve outcomes and reduce morbidity and mortality (7–11). In the present study, we sought to investigate the relationship of duration of hyperglycemia with mortality and ventilator dependence in infants admitted to NICU.

Methods

This retrospective observational study was conducted at Dr. Sheikh Children's Hospital in Mashhad, Iran. Data was obtained from daily medical records of infants aged 0-3 months admitted to this hospital. The studied samples were 112 infants who were admitted to this hospital from October 2015 to December 2015 and were followed up until discharge. The NICU was composed of a heterogeneous population of medical and surgical patients cared for by a team of pediatric intensivists. Information related to blood sugar was collected based on the samples of blood sugar that were routinely taken using a glucometer (Blood Glucose Meter GALA. TD-4277, Taiwan) according to the pediatric intensive care protocol every six hours and was recorded in each patient's blood sugar chart. Glucometer was calibrated according to the relevant instructions for each infant.

In our study, the studied infants were divided into two groups of high blood sugar (BS≥ 126 mg/dl) and normal blood sugar (BS=40-125 mg/dl). Since 80% of the infants in this study were aged less than 30 days, the population was classified as the groups of less than 30 days and more than 30 days. Birth weight was classified into two categories of normal (≥ 2.5 kg) and less than normal (< 2.5 kg) (12).

In our retrospective study, two groups were compared in terms of demographic variables such as age, gender, and birth weight. Variables related to intensive care such as duration of hyperglycemia, ventilator dependence, length of stay in NICU, and treatment outcome (death or discharge) were also compared between the groups, while mortality was separately evaluated. Length of stay could be short due to neonatal mortality. For the purpose of this study, we defined hyperglycemia based on Diabetes Association of America and World Health Organization, which is characterized as the blood glucose level > 126 mg/dl in children (13).

The inclusion criterion for this study was blood sugar ≥ 126 mg/dl at least for once. Duration of hyperglycemia was considered from when blood sugar level reached > 126 mg/dl until blood sugar reached < 126 mg/dl. The mean blood glucose level during this period was considered as an indicator of blood glucose level. All the patients received intravenous sugar solution during hospitalization and none of the infants in our study received insulin to control blood glucose level.

Organ dysfunction was characterized as renal, respiratory, gastrointestinal, and neurological disorders, as well as cancer and septicemia. Descriptive statistics were applied to describe the demographic and descriptive data. Univariate analysis was employed to assess the associations between the risk factors, hyperglycemia, mortality, total number of mechanical ventilation days, and length of hospital stay.

For the outcome measurement, the Kruskal–Wallis test was utilized for independent variables. Statistical analyses were performed in SPSS, version 16. To describe the demographic and descriptive data, descriptive statistics such as mean, standard deviation, median, and interquartile range were used. Since quantitative variables of the study had non-normal distribution, the values of quantitative variables were described as median (interquartile range). Chi-squared test was run to evaluate the association between qualitative variables with groups of blood sugar and mortality. Furthermore, Mann-Whitney test was performed to evaluate the association between the quantitative variables with groups of blood sugar and mortality. P-value less than 0.05 was considered significant. After determining the important factors related to mortality, logistic regression model was conducted for independent factors associated with mortality.

Results

In this study, a total of 112 infants had median

Table 1. The demographic comparison of high and normal blood sugar in 0-3 month old infants

Blood sugar a		n≤125 (%)	n ≥126 (%)	P-value
Gender	Boy	32(55)	31(59.6)	0.62
	Girl	27(45)	21(40.4)	
Age (day)	<30	47(78.3)	42(80.8)	0.75
	≥30	13(21.7)	10(19.7)	
Birth weight (kg)	<2.5	18(30)	23(44.2)	0.11
	≥2.5	42(70)	29(55.8)	

a: Chi-squared
b: Mann-Whitney

Table 2. Comparison of normal and high blood sugar groups based on variables related to intensive care (ventilator dependence, length of hospital stay, and mortality)

Blood sugar a		N=<125 mg/dl	>=126 mg/dl	P-value b
Hyperglycemia duration (hour)		14 (14.75)[c]	24(23.25) [c]	0.009
Long of stay (day)		7.5(13.75)[c]	5(11.75) [c]	0.07
Ventilation	Yes	17(28.3)[d]	34(65.4)[d]	<0.001
	No	43(71.7)	18(34.6)	

a: Chi-square
b: Mann-Whitney
c: Data are expressed as median (interquartile range)
d: n(%)

age of 13 days and median weight of 2.69 kg (57.1% boys and 42.9% girls) and 46.4% of infants (n=52) had hyperglycemia and 53.6% (n=60) had normal blood glucose level. Median and mean of hyperglycemia were 120.5 and 128.05, respectively. Mortality was observed in 31.25% of the infants (n=35). Moreover, 21.42% of the infants (n=24) with hyperglycemia died, and 40.17% of the infants were hospitalized more than 10 days in NICU and mean and median length of hospital stay were 12 and 7 days, respectively (ranging between 1 and 65 days).

The results of the study are presented in tables through evaluation of the relationship between qualitative and quantitative independent variables with blood sugar groups and mortality rate. At first, the relationship between demographic variables, birth weight, mortality, length of hospital stay, and duration of ventilation were compared with the values of high and normal blood sugar (tables 1 and 2). Then, the relationship between these variables and mortality was evaluated (tables 3 and 4). Finally, logistic regression model was used to adjust the confounding variables (tables 5 and 6).

The male to female ratio in the infants with hyperglycemia was 1.47/1. The incidence of hyperglycemia in the infants younger than 30 days was higher than the infants older than 30 days (80.8% vs. 19.7%). The incidence of hyperglycemia

Table 3. The demographic comparison of high and normal blood groups in 0-3 month old infants

Mortality *		Yes number(%)	No number(%)	**P-value
Gender	Boy	20(57.1)	44(57.1)	1
	girl	15(42.9)	33(42.9)	
Age(day)	<30	26(74.3)	63(81.8)	0.36
	≥30	9(25.7)	14(18.2)	
Birth weight(kg)	<2.5	20(57.1)	21(27.3)	0.002
	≥2.5	15(42.9)	56(72.3)	

* Chi-square
**Mann-Whitney

Table 4. Comparison of mortality according to variables related to intensive care

Mortality a		Yes	No	P-value b
Hyperglycemia duration (hour)		30(34)[c]	14(12.5)c	<0.001
Long of stay (day)		5(9)[c]	8(13.5)c	0.03
Ventilation	No	6(27.1)[d]	22(28.6)d	<0.001
	Yes	29(82.9)[d]	55(71.4.)d	
Blood sugar (mg/dl)	≤125	11(31.4)[d]	49(63.6)d	0.002
	≥126	24(68.6)[d]	28(36.4)d	

a: Chi-square
b: Mann-Whitney
c: Median (interquartile range)
d: n(%)

Table 5. Binary variable analysis of the associated factors with mortality using logistic regression model

Mortality		b	SE	Sig a	OR	CI(95%)
Duration		0.049	0.015	0.001	1.05	1.01-1.082
Ventilation	No	-3.15	0.69	<0.001	0.04	0.01-0.016
	Yes		-	-		-
Duration of stay		0.07	0.03	0.01	0. 92	0.87-0.98

a: Logistic regression

Duration of high blood sugar: (P-value=0.001; OR:1.05, CI(95%):1.01-1.08)

Ventilator dependence: (P-value<0.001; OR:0.04, CI(95%):0.01-0.016)

Table 6. Binary variable analysis of the associated factors with ventilator dependence using logistic regression model

Ventilation		b	SE	Sig a	OR	CI(95%)
Duration		0.02	0.01	0.02	1.02	1.003-1.052
Blood sugar	≤125mg/dl	-1. 5	0.43	<0.001	0.21	0.094-0.512
	≥126 mg/dl		-	-		-
Birth weight	<2.5kg	0.87	0.44	0.05	2.3	0.995-5.784
	≥2.5kg		-	-		-

Duration of high blood sugar (P-value=0.02; OR:1.02, CI(95%):1.003-1.052)

Normal blood sugar (P-value<0.001; OR:0.21, CI(95%):0.094-0.512)

in the infants with birth weight < 2.5 kg was lower than the infants with birth weight ≥ 2.5 kg (44.2% vs. 55.8%). The incidence of hyperglycemia showed no significant differences in gender, age, and weight between the groups (Table 1).

The median of hyperglycemia duration was longer in the infants who had average blood sugar of higher than normal (24 hours vs. 14 hours) and the two groups were significantly different in terms of hyperglycemia duration (P=0.009). Ventilator dependence was higher in infants with hyperglycemia (65.5% vs. 34.6%) and the two groups were significantly different in this regard (P<0.001). The median length of NICU stay was shorter in the infants with hyperglycemia (5 vs. 7.5 days) and no significant difference was observed between the two groups in terms of length of stay (Table 2).

Of the studied infants, 35 (31.25%) died. The male to female ratio in the dead infants was 1.33/1; distribution of mortality was similar in both groups. The incidence of mortality was higher in the infants younger than 30 days (74.3% vs. 25.7%) and the age difference was not significant between the dead and survived infants. The incidence of mortality was significantly higher in the infants with low birth weight (57.1% versus 42.9%; P=0.002; Table 3).

In the infants who died, median duration of hyperglycemia was longer (30 hours vs. 14 hours), showing a significant difference with those who survived (P<0.001). According to Table 4, the median length of NICU stay was significantly shorter in the dead infants (5 vs. 8 days) than those who survived (P=0.03). The rate of ventilator dependence was higher in the group of infants who died (82.9% vs. 27.1%); there was a significant difference between dead and survived groups in this respect (P<0.001). Mortality rate was higher in the infants with hyperglycemia (68.6% vs. 31.4%) compared to the infants with normal blood glucose level (P=0.002; Table 4).

Length of hospital stay (P=0.01; OR: 0.92, CI (95%): 0.87-0.98) was identified as an independent factor related to the risk of mortality (Table 5).

Birth weight less than 2.5 kg (P=0.05; OR: 2.3, CI (95%): 0.995-5.748) was identified as independent factor related to the risk of ventilator dependence (Table 6).

Discussion

Since the supply of glucose and its metabolism play a key role in brain development in fetuses and newborns (14) and generally high blood sugar is caused in intensive care due to the impact of clinical interventions not due to disorder in glucose metabolism (15, 16), this study showed the relatively high incidence of blood sugar of higher than normal in NICU infants and emphasizes on the need for monitoring blood glucose in this population. Former studies were performed on blood sugar in pediatrics within a wide age range (4-20), while this study was limited to the infants aged 0-3 months and its results were noteworthy.

Unfortunately, so far no consensus has been made as to the criteria for diagnosis of high blood sugar in NICU infants (15). Some researchers in their studies considered that the criterion for high blood sugar is blood glucose levels of >150 mg/dl or >200 mg/dl and reported its incidence rate to be 16.7-56% in children (2, 21). The studies of Srinivasan et al. (17), Vinayak et al. (4), and

Shirzadeh et al. (22) similar to our study reported that blood sugar > 126 mg/dl is considered as the criterion for high blood sugar.

In the study of Srinivasan et al. (17), the incidence of hyperglycemia was 86% and in the study of Vinayak et al. (4) it was 70%. In our study, the incidence of hyperglycemia was close to the results of Yung et al. (23), which was 46%. In our study, no significant association was observed between the incidence of hyperglycemia and age, gender, and weight of infants; these results were similar to those obtained in the study of Vinyak et al. (4), which was performed on children aged 1 to 12 years old. However, former studies suggested that low birth weight is an important risk factor for the incidence of hyperglycemia in infants (24) and its incidence ranges from 2% in infants who have birth weight > 2 kg to 45% in the infants with birth weight <1 kg (25).

We noticed that duration of hyperglycemia stability was longer in infants with blood glucose level of higher than normal; no similar result was observed in other studies. Although length of NICU stay was shorter in the infants who had hyperglycemia, our study showed no significant differences between the two groups in terms of length of hospital stay. However, in the studies of Wintergerest et al. (26) and Branco et al. (27), duration of hospitalization was associated with maximum high blood sugar. Duration of hospitalization may be shorter because of infant's death due to hyperglycemia.

Relationship between mortality and high blood sugar

In our study, mortality rate was higher in the group who had high blood sugar (68.6% vs. 31.4%) and similar results were found in the studies of Wintergerest et al. (26) and Vinayak et al. (4). However, in our study rate of mortality in infants who had high blood sugar was more ostensible than other studies. Perhaps, it is due to the vulnerability of the infants aged 0-3 months compared to other children with regards to fluctuations in blood glucose level. In former studies, the results indicated that the maximum blood sugar is associated with increased risk of mortality (2, 4, 10, 17).

In our study, when logistic regression model was performed for the impact of high blood sugar on mortality, average blood sugar level of higher than 126 mg/dl was not shown as an independent factor impacting the incidence of mortality. In our study, we considered average blood sugar from when it was higher than 126 mg/dl until it reached lower than 126 mg/dl, whereas in other studies, the maximum blood sugar during this period was applied (4, 17, 23).

However, in a study by Yanhong Li et al. in 2015 on children hospitalized in the intensive care unit, the results showed that blood sugar levels between 110 to 140 were associated with lower risk of mortality, and blood glucose cut-off higher than 140 was associated with 4.13 times higher chance of death (28). In our study, only 21.42% of the infants had died and median of blood sugar in our infants was 120.5 mg/dl with mean of 128.5 mg/dl, which is not high compared with other studies, this amount according to the study of Yanhong (28) et al. shows a weak relationship with mortality.

Relationship between mortality and duration of hyperglycemia

The studies of Faustino et al. (19), Hirshberg et al. (29), and Srinivasan et al. (17) pinpointed the relationship between duration of hyperglycemia in PICU and mortality; in the study of Srinivasan et al. (17), blood sugar level greater than 126 mg/dl was associated with six times increased risk of mortality in children. In our study, the results showed that when the hours of blood sugar levels higher than normal accrues, the probability of death increases (P=0.001), such that each one hour increment in high blood glucose level leads to 1.5 times increase in the chance of mortality.

Mechanical ventilation

In this study, the effect of risk factors on ventilator dependence and the effect of ventilation on the incidence of mortality were evaluated. In our observation similar to those of Srinivasan et al. (17), Yung et al. (23), and Branco et al. (18) on children and infants, the need for ventilation was higher in infants with hyperglycemia. The results of Branco et al. study on ventilator dependence in NICU infants showed that the need for ventilation can be related to the effects of high blood sugar on the inefficiency of the respiratory system (18). The stress response to acute illness leads to the release of stress hormones such as epinephrine and catecholamine and can elevate blood glucose level, especially in infants who are ventilator dependent (14).

Yates et al. also showed that prolonged hyperglycemia is associated with elongated duration of ventilator dependence (30). In

congruence with that study, our study demonstrated that in infants with hyperglycemia, every hour increase in hyperglycemia duration leads to 1.02 times increase in ventilator dependence (P=0.02).

Day et al. observed that among children with meningococcemia, ventilator dependence was less in children who had lower blood glucose level (31). Our results revealed that among infants who had normal average blood sugar, the chance of ventilator dependence was 0.21 times less than the other groups.

In the evaluation of the effect of birth weight on ventilator dependence in our study, we observed that birth weight has a relatively significant impact on ventilator dependence, such that for every kilogram decrease in birth weight compared to normal values, the risk of ventilator dependence increases by 2.3 times (P=0.05).

Interestingly, in our study, ventilator dependence was an independent factor in the occurrence of neonatal mortality, such that in the groups who were ventilator independent, the risk of mortality was 0.05 times less than ventilator dependent group (P<0.001); nonetheless, such a relationship was not observed between ventilator dependence and the incidence of mortality in the study by Srinivasan et al. (17).

Relationship between mortality and length of stay

It was noted that for each day increase in hospital stay, the chance of mortality raises by 0.92 times in the infants aged 0-3 months (P=0.01). Similar to the results of our study, Pollack et al. showed that the length of stay in PICU escalates the risk of mortality (17.4% vs. 7.3%; P<0.05) (32).

Conclusion

Glycemic control in the infants admitted to NICU is challenging, because at this time, the infant is complicated with simultaneous disorders in multiple organs (14). Hyperglycemia is defined as complete blood sugar higher than 120 to 125 mg/dl or plasma sugar concentration higher than 145 to 150 mg/dl regardless of gestational age, weight, or age after birth (25).

In most cases, the complicated infant has no signs and symptoms different from the signs of disease; the only diagnosable factor is duration of continuity of osmotic urine (presence of sugar in urine), weight loss, impaired growth, fever, glucose excretion from urine, ketosis, and metabolic acidosis (25). Given the low reliability of clinical signs for detecting hyperglycemia and the importance of blood sugar management, it is required to constantly control and monitor blood sugar (33).

Various studies reported different findings regarding the prevalence of blood sugar in infants admitted to NICU. In our study, cut-off mean blood sugar level was considered higher than normal (126 mg/dl) and had no significant relationship with the incidence of death; however, the results showed that death in the infants aged 0-3 months can have a direct association with duration of hyperglycemia and an inverse relationship with ventilator independence. In addition, duration of hyperglycemia and low birth weight can have a direct link with ventilator dependence and an inverse relationship with average of normal blood sugar.

Limitations of the study

In the present study, blood glucose of infants was measured using glucometer and through measurement of complete blood sugar. Glucometer is not a reliable tool, but it is more applicable due to easy assessment and no need for high amount of blood. Since the concentration of red blood cells in human is half of their concentration in plasma, assessment of glucose through complete blood is 10-15% less than what is obtained in the assessment of serum or plasma glucose using automatic analyzer. In case of hematocrit concentration of higher than normal, which is usually seen in the ill newborns, glucose in complete blood may be less (34). Therefore, it is better to use automatic analyzer or serum or plasma sample for the assessment of blood sugar in NICUs.

Acknowledgments

The authors appreciate the cooperation Dr. Pouryazdanpanah for her continued interest and involvement in the study.

Conflicts of interests

None declared.

References

1. Kyle UG, Coss Bu JA, Kennedy CE, Jefferson LS. Organ dysfunction is associated with hyperglycemia in critically ill children. Intensive Care Med. 2010; 36(2):312-20.
2. Klein GW, Hojsak JM, Schmeidler J, Rapaport R. Hyperglycemia and outcome in the pediatric intensive care unit. J Pediatr. 2008; 153(3):379-84.
3. Preissig CM, Rigby MR. A disparity between physician attitudes and practice regarding

hyperglycemia in pediatric intensive care units in the United States: a survey on actual practice habits. Crit Care. 2010; 14(1):R11.
4. Patki VK, Chougule SB. Hyperglycemia in critically ill children. Indian J Crit Care Med. 2014; 18(1):8-13.
5. Poddar B. Treating hyperglycemia in the critically ill child: is there enough evidence? Indian Pediatr. 2011; 48(7):531-6.
6. Naranje KM, Poddar B, Bhriguvanshi A, Lal R, Azim A, Singh RK, Gurjar M, et al. Blood glucose variability and outcomes in critically ill children. Indian J Crit Care Med. 2017; 21(3):122-6.
7. Kao LS, Morris BH, Lally KP, Stewart CD, Huseby V, Kennedy KA. Hyperglycemia and morbidity and mortality in extremely low birth weight infants. J Perinatol. 2006; 26(12):730-6.
8. Hirshberg E, Lacroix J, Sward K, Willson D, Morris AH. Blood glucose control in critically ill adults and children: a survey on stated practice. Chest. 2008; 133(6):1328-35.
9. Nayak P, Lang H, Parslow R, Davies P, Morris K. Hyperglycemia and insulin therapy in the critically ill child. Pediatr Criti Care Med. 2009; 10(3):303-5.
10. Hall NJ, Peters M, Eaton S, Pierro A. Hyperglycemia is associated with increased morbidity and mortality rates in neonates with necrotizing enterocolitis. J Pediatr Surg. 2004; 39(6):898-901.
11. Vlasselaers D, Milants I, Desmet L, Wouters PJ, Vanhorebeek I, van den Heuvel I, et al. Intensive insulin therapy for patients in paediatric intensive care: a prospective, randomised controlled study. Lancet. 2009; 373(9663):547-56.
12. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. Champaign, IL: Human Kinetics Books; 1988.
13. Moghissi ES, Korytkowski MT, DiNardo M, Einhorn D, Hellman R, Hirsch IB, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. Diabetes Care. 2009; 32(6): 1119-31.
14. Shaffner DH, Nichols DG. Rogers' textbook of pediatric intensive care. Philadelphia: Lippincott Williams & Wilkins; 2015.
15. Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Parenteral Nutrition Guidelines Working Group, et al. 1. Guidelines on paediatric parenteral nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), supported by the European Society of Paediatric Research (ESPR). J Pediatr Gastroenterol Nutr. 2005; 41(Suppl 4):S1-87.
16. Schlebusch H, Niesen M, Sorger M, Paffenholz I, Fahnenstich H. Blood sugar determinations in newborns: four instruments compared. Pediatr Pathol Lab Med. 1998; 18(1):41-8.
17. Srinivasan V, Spinella PC, Drott HR, Roth CL, Helfaer MA, Nadkarni V. Association of timing, duration, and intensity of hyperglycemia with intensive care unit mortality in critically ill children. Pediatr Crit Care Med. 2004; 5(4):329-36.
18. Branco RG, Tasker RC. Glycemic level in mechanically ventilated children with bronchiolitis. Pediatr Crit Care Med. 2007; 8(6):546-50.
19. Faustino EV, Apkon M. Persistent hyperglycemia in critically ill children. J Pediatr. 2005; 146(1):30-4.
20. Macrae D, Grieve R, Allen E, Sadique Z, Morris K, Pappachan J, et al. A randomized trial of hyperglycemic control in pediatric intensive care. N Engl J Med. 2014; 370(2):107-18.
21. McCowen KC, Malhotra A, Bistrian BR. Stress-induced hyperglycemia. Crit Care Clin. 2001; 17(1):107-24.
22. Shirzadeh L, Nasrfard S, Abdollahpour N, Khademi G, Sezavar M. Investigation of the relation between hyperglycemia and morbidity and mortality rates in critically Ill children in March 2013 to February 2014. Razavi Int J Med. 2016; 4(4):e40340.
23. Yung M, Wilkins B, Norton L, Slater A; Paediatric Study Group; Australian and New Zealand Intensive Care Society. Glucose Sugar control, organ failure, and mortality in pediatric intensive care. Pediatr Crit Care Med. 2008; 9(2):147-52.
24. Catre D, Lopes MF, Madrigal A, Oliveiros B, Viana JS, Cabrita AS. Early mortality after neonatal surgery: analysis of risk factors in an optimized health care system for the surgical newborn. Rev Bras Epidemiol. 2013; 16(4):943-52.
25. Hemachandra AH, Cowett RM. Neonatal hyperglycemia. Pediatr Rev. 1999; 20(7):16.
26. Wintergerst KA, Buckingham B, Gandrud L, Wong BJ, Kache S, Wilson DM. Association of hypoglycemia, hyperglycemia ,and sugar variability with morbidity and death in the pediatric intensive care unit. Pediatrics. 2006; 118(1):173-9.
27. Branco RG, Garcia PC, Piva JP, Casartelli CH, Seibel V, Tasker RC. Glucose level and risk of mortality in pediatric septic shock. Pediatr Crit Care Med. 2005; 6(4):470-2.
28. Li Y, Bai Z, Li M, Wang X, Pan J, Li X, et al. U-shaped relationship between early blood sugar and mortality in critically ill children. BMC Pediatr. 2015; 15(1):88.
29. Hirshberg E, Larsen G, Van Duker H. Alterations in sugar homeostasis in the pediatric intensive care unit: Hyperglycemia and sugar variability are associated with increased mortality and morbidity. Pediatr Crit Care Med. 2008; 9(4):361-6.
30. Yates AR, Dyke PC 2nd, Taeed R, Hoffman TM, Hayes J, Feltes TF. et al. Hyperglycemia is a marker for poor outcome in the postoperative pediatric cardiac patient. Pediatr Crit Care Med. 2006; 7(4):351-5.
31. Day KM, Haub N, Betts H, Inwald DP. Hyperglycemia is associated with morbidity in critically ill children with meningococcal sepsis. Pediatr Crit Care Med. 2008; 9(6):636-40.
32. Pollack MM, Wilkinson JD, Glass NL. Long-stay pediatric intensive care unit patients: outcome and resource utilization. Pediatrics. 1987; 80(6):855-60.
33. Wu Y, Pei J, Yang XD, Cheng ZD, Zhao YY, Xiang B.

Hyperglycemia and its association with clinical outcomes for patients in the pediatric intensive care unit after abdominal surgery. J Pediatr Surg. 2013; 48(4):801-5.