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ORIGINAL ARTICLE

Hyperglycemia as a prognostic factor for increased mortality in patients admitted in Pediatric ICU.

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ABSTRACT… Objective: To study the prevalence and frequency of hyperglycemia in critically ill children. To juxtapose mortality rate in critically ill patients with hyperglycemia against those having normal blood glucose levels. **Study Design:** Descriptive Case Series. **Setting:** Pediatric Intensive Care Unit (PICU) of HITEC, IMS Taxila, Al-Ihsan Hospital Rawalpindi & Hameed Latif Teaching Hospital, Lahore. **Period:** March 2023 to October 2023. **Methods:** One hundred critically ill children admitted to PICU were included. Patients who had blood glucose levels more than 150mg/dl within 48 hours of admission were included in the hyperglycemic group (Group A).Patients with normal blood sugars were included in Group B. The normoglycemic and hyperglycemic groups were followed till 10 days to determine the mortality associated with hyperglycemia. **Results:** Mean age of the children was 6.7± 6.29 months. There were 72% male children and 28% female children. Mean blood glucose levels at baseline, after 24h hours, after 36 hours and after 48 hours were 194.91± 135.66mg/dl, 156.91±74.89mg/dl, 156.21 ±83.05mg/dl and 150.13±70.68mg/dl. Frequency of hyperglycemia was observed in 55% (n= 55). Mortality rate was 43% (n= 43/100). Furthermore, mortality rate was crucially inflated 63.6% (n= 35) in hyperglycemic victims than normoglycemic patients (p=<0.001). **Conclusion:** Frequency of high blood sugar along with mortality within 10 days of hospitalization in children with hyperglyceemia was found higher in patients admitted to Pediatric ICU.

Key words: Critically Ill Children, High Blood Sugar, Mortality.

INTRODUCTION

Severe critical illness is linked to increased blood sugar levels, referred to as stress hyperglycemia or critical illness hyperglycemia.[1] Based on the recent consensus from the American Diabetes Association and the American Association of Clinical Endocrinologists, stress hyperglycemia is characterized as any temporary plasma glucose levels exceeding 140 mg/dL during episodes of acute physical or psychological stress, without indications of pre-existing diabetes.[2] Managing glucose is a crucial aspect of intensive care. Typically, irregularities in blood glucose are associated with adverse outcomes in critically ill patients and represent a complication that affects multiple systems.[3] A study conducted in China concluded that out of 780 participants, 12.4% (n = 97) expired within 28 days admission. Significant statistical differences were observed between survivors and non-survivors based on four glucose variability metrics.[3]

Research indicates that glycemic variability has a more adverse impact compared to persistent chronic hyperglycemia and is linked to multiple organ dysfunctions, especially neurological impairment.[4] The primary mechanism behind SH is attributed to enhanced gluconeogenesis and glycogenolysis, coupled with insulin resistance triggered by proinflammatory cytokines and counter-regulatory hormones released during critical illness.[5] It has been found that stress hyperglycemia is prevalent among children experiencing acute illnesses and correlates with increased rates of hospitalization and mortality.[5] Apart from changes in glucose metabolism and the development of insulin resistance due to inflammation and organ dysfunction, certain

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interventions within the intensive care unit can also impact glucose balance and stress hyperglycemia during severe illness.[6]

A study conducted by Srinavasan et al revealed that severe hyperglycemia in the initial hours and its prolonged duration have been identified in patients who died in Pediatric ICU. 86% of the patients who had hyperglycemia during their hospital stay were related to increased mortality.[7] Appropriate management of hyperglycemia in the context of critically ill patients, including those in the pediatric population, can contribute to improved outcomes and a more favorable course of recovery in the subsequent days.

The rationale of our study is to study the outcome of severely sick children with hyperglycemia in Peadiatric ICU setup because hyperglycemia is more dangerous than hypoglycemia in these patients. It will help in managing children at risk.

METHODS

The study was conducted in PICU of HITEC, IMS Taxila, Al-Ihsan Hospital Rawalpindi & Hameed Latif Teaching Hospital Lahore. Study duration was from March 2023 to October 2023 after approval from ethical committee (AIH/MS/00107/2312/23). It was a descriptive case series. Patients were enrolled via non-probability consecutive sampling. The sample size was 100 patients admitted in PICU within age bracket of 1 month to 12 years. All patients fulfilling the inclusion criteria were included in the study and were admitted in PICU. Blood sugar levels were monitored and checked at admission by glucometer (Easy Gluco) once and again quotidian for 48 hours.

The findings were consistently calibrated, and counter checked from the laboratory. Patients with blood sugar greater than 150mg/dl were appended in hyperglycemia group designated as Group A where as the patients having normal blood sugar levels were considered in normoglycemia group designated as Group B. The gravity of illness was determined using pediatric risk of mortality score (PRISM II).

Insulin-dependent children with fulminant hepatic failure, children with kidney failure in need of dialysis, children with infusion of dextrose containing fluids up to 2 hours prior to admission and children on steroids were excluded from the study. Data interpretation was finalized using SPSS version 17.

Mean and standard deviation was calculated for numerical variables. Categorical variables like gender, hyperglycemia and mortality were presented as frequency and percentage. Data was presented in the form of tables. Data was stratified for age, gender, weight and blood glucose levels. Post stratification chi-square test was performed keeping a P-Value < 0.05 as significant.

RESULTS

This study examined 100 patients of each gender. Majority of the children (68%) were below 8 months of age. Out of 100 patients there were 72 males and 28 females. Mean PRISM Score II of the children was 27.63 ± 18.54. Mean blood glucose level at baseline after 24 hours, after 36 hours and after 48 hours was 194.91 (±) 135.66 mg/dl, 156.91 (±) 74.89 mg/dl, 156.21 (±) 83.05 mg/dl, and 150.13 (±) 70.68 mg/dl.

Hyperglycemia was observed in 55% severely ill children. Mortality rate was 43% (n = 43/100). However, it was remarkably high in hyperglycemic patients yet less in non-hyperglycemic patients 35 (63.6%) vs. 8 (17.8%) P=<0.001. (Results are summarized in Table-I, II and III)

Characteristics		Group A N (%)	Group B N (%)	P-Value
Age Group (months)	≤8	35(63.6)	33(73.3)	0.301
	>8	20(36.4)	12(26.7)	
Gender	Male	39(70.9)	33(73.3)	0.788
	Female	16(29.1)	12 (26.7)	
Weight	≤8 kg	35(63.6)	37(82.2)	0.039
	≥ 8kg	20(36.4)	8(17.8)	
Prism score	≤30	47(85.5	8 17.8	<0.001
	>30	8 (14.5)	37 (82.2)	

Table-I. Comparison of hyperglycemia with general characteristics of the patients (n=100)

Group	Mortality		Total	P- Value
	Yes	No		
A	35 (63.6)	20 (36.4)	55 (100)	<0.001
B	8 (17.8)	37 (82.2)	45 (100)	

Table-II. Comparison of mortality during hospitalization within 10 days in patients with or without hyperglycemia (n=100)

Characteristic		Patient Group	Mortality		P- Value
			Yes n (%)	No n (%)	
Age group (in months)	≤8	A	19 (54.3)	16 (45.7)	0.011
		B	8 (24.2)	25 (75.8)	
	>8	A	16 (80)	4 (20)	<0.001
		B	0 (0)	12 (100)	
Gender	Male	A	27 (69.2)	12 (30.8)	<0.001
		B	8 (24.2)	25 (75.8)	
	Female	A	8 (50)	8 (50)	0.004
		B	0(0)	12 (100)	
Weight	≤8	A	23 (65.7)	12 (34.3)	<0.001
		B	8 (21.6)	29 (78.4)	
	>8	A	12 (60)	8 (40)	0.004
		B	0 (0)	8 (100)	
Prism score	≤30	A	35 (74.5)	12 (25.5)	0.106
		B	8 (100)	0 (0)	
	>30	A	0 (0)	8 (100)	-
		B	0 (0)	37 (100)	

Table-III. Comparison of mortality during hospitalization within 10 days in patients with or without hyperglycemia with general characteristics of the patients (n=100)

DISCUSSION

Hyperglycemia has been identified as an important negative prognostic factor, particularly in the context of critically ill patients in the intensive care unit (ICU). Numerous studies have demonstrated a strong association between hyperglycemia and increased morbidity and mortality rates among adult patients.

In this study 100 children were recruited which included predominantly boys (72%). Hyperglycemia was observed in some of critically ill children (53%) and mortality rate was raised (63.6%). Additionally, mortality of critically ill children with hyperglycemia was statistically significant (P=<0.001). A study by Srinivasan et all concluded that severe hyperglycemia within the initial 48 hours in the PICU correlated with a threefold rise in the risk of mortality among critically ill patients.[7]

Stress induced hyperglycemia leads to insulin resistance and elevated blood glucose levels. Counter regulatory hormones such as catecholamines, cortisol, glucagon, and growth hormone disrupt glucose regulation. Additionally, heightened levels of inflammatory cytokines exacerbate the metabolic environment. Consequently, hepatic gluconeogenesis becomes unregulated. The uptake of glucose by skeletal muscles through the glucose transporter type 4 (GLUT-4) is compromised. Moreover, insulin levels are insufficient to counteract the hyperglycemic state.[8]

The impact of hyperglycemia on the brain is significant, and it is particularly pronounced in conditions such as acute brain injury, where it is linked to increased risks of death and poor functional recovery in survivors. Additionally, in cerebral ischemia, hyperglycemia is associated with specific detrimental effects on the ischemic brain tissue. Hyperglycemia has been shown to exacerbate cerebral tissue damage and edema, enlarging the area of infarction.[9]

The NICE-SUGAR trial was a large, multicenter study involving 6,104 medical and surgical patients admitted to ICUs across 42 hospitals in Australia, New Zealand, Canada, and the United States. The study concluded that intensive insulin therapy targeting lower blood glucose levels (81-108 mg/dL) did not result in improved

outcomes in terms of morbidity when compared to conventional insulin therapy targeting higher blood glucose levels (≤180 mg/dL).[10]

It remains uncertain whether hyperglycemia serves as an indicator of severe illness in children or acts as a causative factor leading to unfavorable outcomes. A study conducted by Vinayak et all concluded that out of 101 critically ill children admitted in Paediatric ICU 69.3% exhibited hyperglycemia. Those with hyperglycemia had a higher need for ventilation (32.9%), a greater necessity for inotropic support (38.6%), a longer average stay in the PICU (7.91 ± 5.01 days) and a higher mortality rate (28.6%) compared to those without hyperglycemia. These differences were statistically significant ($P < 0.05$).[11]

Concerns about the risk of insulin-induced hypoglycemia have been a significant consideration in the pediatric intensive care setting.[12] The approach to glycemic control in critically ill children remains an area of active research, and consensus guidelines may continue to evolve.

CONCLUSION

Frequency of hyperglycemia as well as mortality within 10 days of hospitalization in children with hyperglycemia was found higher in children admitted at pediatric ICU of three hospitals. There is a need to implement monitoring of blood glucose in critically ill pediatric patients in intensive care units.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Becker CD, Sabang RL, Nogueira Cordeiro MF, Hassan IF, Goldberg MD, Scurlock CS. Hyperglycemia in medically critically ill patients: Risk factors and clinical outcomes. Am J Med [Internet]. 2020; 133(10):e568–74. Available from: https://www.sciencedirect.com/science/article/pii/S0002934320302436

2. Korakas E, Argyropoulos T, Koliou G-A, Gikas A, Kountouri A, Nikolopoulou SK, et al. **Prevalence and prognostic factors of stress hyperglycemia in a pediatric population with acute illness in Greece—A prospective observational study.** J Clin Med [Internet]. 2022 [cited 2023 Dec 26]; 11(5):1301. Available from: https://www.mdpi.com/2077-0383/11/5/1301

3. Dong M, Liu W, Luo Y, Li J, Huang B, Zou Y, et al. **Glycemic variability is independently associated with poor prognosis in five pediatric ICU centers in southwest China.** Front Nutr [Internet]. 2022; 9. Available from: http://dx.doi.org/10.3389/fnut.2022.757982

4. Du Y, Liu C, Li J, Dang H, Zhou F, Sun Y, et al. **Glycemic variability: An independent predictor of mortality and the impact of age in pediatric intensive care unit.** Front Pediatr [Internet]. 2020; 8. Available from: http://dx.doi.org/10.3389/fped.2020.00403

5. Bae W, Ahn MB. Association between stress hyperglycemia and adverse outcomes in children visiting the pediatric emergency department. Children (Basel) [Internet]. 2022 [cited 2023 Dec 26]; 9(4):505. Available from: https://www.mdpi.com/2227-9067/9/4/505

6. Srinivasan V. **Glucose metabolism and stress hyperglycemia in critically ill children.** Indian J Pediatr [Internet]. 2023; 90(3):272-9. Available from: http://dx.doi.org/10.1007/s12098-022-04439-y

7. 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 [Internet]. 2004 [cited 2023 Dec 27]; 5(4):329-36. Available from: https://pubmed.ncbi.nlm.nih.gov/15215001/

8. Vedantam D, Poman DS, Motwani L, Asif N, Patel A, Anne KK. **Stress-induced hyperglycemia: Consequences and management.** Cureus [Internet]. 2022 [cited 2023 Dec 27]; 14(7). Available from: https://www.cureus.com/articles/100945-stress-induced-hyperglycemia-consequences-and-management#!/

9. Zhang H, Yue K, Jiang Z, Wu X, Li X, Luo P, et al. **Incidence of stress-induced hyperglycemia in acute ischemic stroke: A systematic review and meta-analysis.** Brain Sci [Internet]. 2023 [cited 2023 Dec 27]; 13(4):556. Available from: https://www.mdpi.com/2076-3425/13/4/556

10. Finfer S, Chittock DR, Su SY, Blair D, Foster D, Dhingra V, et al. **Intensive versus conventional glucose control in critically ill patients.** N Engl J Med [Internet]. 2009 [cited 2023 Dec 27]; 360(13):1283-97. Available from: https://pubmed.ncbi.nlm.nih.gov/19318384/

11. Patki VK, Chougule SB. **Hyperglycemia in critically ill children.** Indian J Crit Care Med [Internet]. 2014 [cited 2023 Dec 27]; 18(1):8-13. Available from: http://dx.doi.org/10.4103/0972-5229.125427

12. Faustino EVS, Hirshberg EL, Bogue CW. **Hypoglycemia in critically ill children.** J Diabetes Sci Technol [Internet]. 2012 [cited 2023 Dec 27]; 6(1):48-57. Available from: http://dx.doi.org/10.1177/193229681200600107

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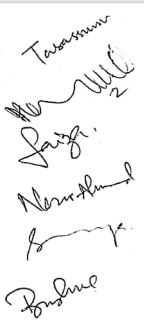
1	Tabassum Fatima	Data collection, Writing introduction.	
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