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Dr. Sheeba
PG Resident, Department of Paediatrics, Study performed in Rohilkhand Medical College, Bareilly, UP in Department of Pediatrics, Bareilly, Uttar Pradesh, India

Dr. Rajesh Bansal
Prof. HOD Department. Of Pediatrics, Study Performed in Rohilkhand Medical College, Bareilly, UP in Department of Pediatrics, Uttar Pradesh, India

Dr. Atul Shishodia
SR, Department. of General Surgery Study Performed in Rohilkhand Medical College, Bareilly, UP in Department of Pediatrics, Uttar Pradesh, India

Correspondence
Dr. Sheeba
PG Resident, Department of Paediatrics, Study performed in Rohilkhand Medical College, Bareilly, UP in Department of Pediatrics, Bareilly, Uttar Pradesh, India

Correlation of plasma glucose level with morbidity and mortality in pediatric intensive care unit patient

Dr. Sheeba, Dr. Rajesh Bansal and Dr. Atul Shishodia

Abstract
This study was conducted in PICU of rohilkh and medical college.
Aim: to study the relationship between plasma glucose level and morbidity and mortality outcome in PICU patients.
Material and Methods: Plasma sugar was assessed using auto analyser (Erba) using glucose oxidase method in blood samples taken at 0, 12, 24hrs.
Results: On evaluating the association between outcome and glycemic status (Normoglycemic, hypoglycemic and hyperglycemic) at different time intervals, majority of normoglycemic and hyperglycemic patients were either discharged after recovery or were referred to higher facility while majority of hypoglycemic patients expired.
Conclusion: there was a significant association between glycemic status and outcome.

Keywords: plasma sugar, hyperglycemia, hypoglycemia, normoglycemia

Introduction
Hyperglycemia is common in critically ill patients and appears to be a marker of disease severity.
Prevalence of stress hyperglycemia in critically ill patients has been reported to range from 15% to 86% [1-4]. It has been shown in several clinical studies that hyperglycemia is a risk factor for adverse outcomes during acute illness.
On the other hand, adverse effects of hypoglycemia have also been well documented in the pediatric literature [5-7]. In fact, glucose being an important substrate for energy; maintenance of its blood levels is of critical importance. Till recently, great amount of attention has been paid to avoidance and early treatment of hypoglycaemia [8]. As hyperglycemia was considered to be an adaptive response to stress; scant attention was paid to its occurrence, prevention or treatment3. The situation seems to be changing slowly [9, 10]. Variability in glucose levels is being increasingly recognized as an important factor influencing the outcome in terms of prolonged hospital stay, prevalence of organ dysfunction and mortality.
In view of the above clinical evidences, it can be understood that both hyperglycemia as well as hypoglycemia can play a detrimental role in affecting the outcome of critically ill children admitted to a pediatric intensive care unit. Targeting blood glucose levels in the 'normal' range; i.e. <110 mg/dL is difficult, increases nursing activity significantly [11] and is fraught with the risk of hypoglycemia. It is more appropriate to target a level of 110-150 mg/dL [12, 13]. With this range of blood glucose, the ill effects of hyperglycemia are overcome while avoiding the dangers and difficulty of achieving normoglycemia.
The present study was proposed to determine the correlation between plasma glucose level and the outcome in pediatric intensive care unit of a tertiary care hospital in north India.

Material and Method
Setting: Hospital based, observational study.
Study Area: Pediatric Intensive Care Unit of Rohilkhand Medical College, Bareilly.
Study Design: Observational cross section study
Study Population: Children admitted to PICU, Rohilkhand Medical College & Hospital.

Inclusion Criteria
Sick children, aged 1-15 years, admitted to the PICU.

Exclusion Criteria

- Patients with Diabetes mellitus type 1 and 2 diagnosed before or after admission.
- Patients receiving drugs like corticosteroids.
- Patients received i.v dextrose within 24 hrs prior to the admission.
- Patients who expired within 24 hours. Patients referred to higher centre within 24 hrs of admission.
- Patients whose attendants refused for informed consent.

Method

All sick patients admitted in PICU, fulfilling the specified inclusion criteria, were assessed for eligibility. Those who did not come under the specified exclusion criteria were enrolled for the study after obtaining written & informed consent. After initial evaluation, 2ml of blood was withdrawn in addition to routine samples and stored in fluoride vial and was sent for plasma glucose assessment. Patient was then treated according to specific etiology using standard protocol. Subsequently, blood samples were also obtained at 12 hours and 24 hours of admission. These patients were then followed till they were shifted out from PICU.

Outcome was defined as

- Discharged/Shifted to ward
- Referred to higher centre/Deteriorated
- Leave against medical advice
- Expired

Study Instruments: A pre-designed study proforma was used to collect data.

Plasma sugar was assessed using autoanalyser (erba) using glucose oxidase method. The following criteria was used for classifying glucose levels:

Glucose level	Category
<60 mg/dl	Hypoglycemia
60-125 mg/dl	Normal
≥126 mg/dl	Hyperglycemia

Highest / lowest value of the three measurements was taken as the representative category.

Data Analysis

All the data was then entered in MS Excel spreadsheet and analyzed using Statistical Package for Social Sciences (SPSS) version 21.0. Chi-square test, ANOVA and independent samples 't'-test was used to analyze the data. A 'p' value less than 0.05 was considered as statistically significant.

Results

All the sick children aged upto 15 years of age admitted in PICU were invited to participate in the study, of these 90 fulfilling inclusion criteria and giving consent for the study were enrolled as study subjects. Demographic details of the patients enrolled in the study is given in Table 1.

Table 1: Distribution of Study Population according to Demographic Variables

S. No.	Demographic Variables	Number of patients	Percentage
1	**Age Group**		
	<1 year	40	44.4
	1-5 years	15	16.7
	6-10 years	10	11.1
	>10 years	25	27.8
	Min-Max (Median):	2 months to 15 years (2 years)	
	Mean±SD	5.28±5.56 years	
2	**Gender**		
	Female	35	38.9
	Male	55	61.1

Age of pediatric patients in PICU ranged between 2 months to 15 years (median 2 years) and mean age of patients was 5.28±5.56 years. Maximum patients were <1 year of age (44.4%).

Majority of the patients admitted in PICU were males (61.1%). Gender ratio (M:F) was 1.57.

On systemic examination, respiratory abnormalities were most common (n=56; 62.2%) followed by gastrointestinal abnormalities (n=25; 17.8%), cardiovascular abnormalities (17.8%) and low GCS (n=7; 7.8%) respectively.

Table 6: Distribution of Study Population according to etiology

S. No.	Etiology	Number of patients	Percentage
1.	Respiratory system (RS)	30	33.3
2.	Central nervous system (CNS)	15	16.7
3.	Infections	11	12.2
4.	Cardiovascular system (CVS)	9	10.0
5.	Hematological with CVS	6	6.7
6.	Hematological	4	4.4
7.	Gastrointestinal	4	4.4
8.	Trauma	4	4.4
9.	Burn	3	3.3
10.	Postoperative	2	2.2
11.	Renal	1	1.1
12.	Poisoning	1	1.1

Respiratory system (n=30; 33.3%) was most commonly involved, followed by central nervous system (n=15; 16.7%). There were 11 (12.2%) patients with infectious etiology. A total of 9 (10%) had cardiovascular involvement while 6 (6.7%) had hematological with CVS involvement. A total of 4 (4.4%) cases each had hematological, gastrointestinal and traumatic etiology. Three (3.3%) cases had burn etiology. A total of 2 (2.2%) cases were post-operative complications and 1 (1.1%) each had renal and poisoning etiologies.

Table 12: Correlation of Outcome and Plasma Glucose Status at different periods of observation

S.No.	Time of observation	Discharged (n=44)		Expired (n=28)		Referred to higher facility (n=11)		Statistical significance	
		No.	%	No.	%	No.	%	χ^2	'p'
1.	At admission								
	Normoglycemic (n=31)	16	51.6	6	19.4	9	29.0	22.09	<0.001
	Hypoglycemic (n=10)	1	10.0	7	70.0	2	20.0		
	Hyperglycemic (n=42)	27	64.3	15	35.7	0	0		
2.	At 12 h								
	Normoglycemic (n=30)	16	53.3	6	20.0	8	26.7	16.84	<0.001
	Hypoglycemic (n=9)	1	11.1	6	66.7	2	22.2		
	Hyperglycemic (n=44)	27	61.4	16	36.4	1	2.3		
3.	At 24 h								
	Normoglycemic (n=30)	18	60.0	4	13.3	8	26.7	22.01	<0.001
	Hypoglycemic (n=8)	0	0	6	75.0	2	25.0		
	Hyperglycemic (n=45)	26	57.8	18	40.0	1	2.2		

Percentages have been calculated row-wise

Mortality rate for at admission normoglycemic, hypoglycemic and hyperglycemic patients was 19.4%, 70% and 35.7% respectively while referral rate was 29%, 20% and 0% respectively. The discharge rate was 51.6%, 10% and 64.3% respectively for normoglycemic, hypoglycemic and hyperglycemic patients. Statistically, there was a significant association between at admission plasma glucose levels and outcome (p<0.001).

Table 14: Correlation of Mechanical Ventilation need and Deranged Plasma Glucose Status at different periods of observation (n=90)

S. No.	Time of observation	MV Needed (n=35)		MV Not needed (n=55)		Statistical significance	
		No.	%	No.	%	χ^2	'p'
1.	At admission						
	Normoglycemic (n=33)	6	18.2	27	81.8	9.40	0.002
	Deranged (n=57)	29	50.9	28	49.1		
2.	At 12 h						
	Normoglycemic (n=32)	8	25.0	24	75.0	4.03	0.045
	Deranged (n=58)	27	46.6	31	53.4		
3.	At 24 h						
	Normoglycemic (n=31)	8	25.8	23	74.2	3.41	0.065
	Deranged (n=59)	27	45.8	32	54.2		

Percentages have been calculated row-wise

At all the three time intervals, MV need was higher among those with deranged plasma glucose levels as compared to those having glucose levels in normal range. However, the association was significant statistically only for at admission and at 12 hour glucose levels (p<0.05).

Table 17: Plasma Glucose levels and Duration of ICU/Hospital Stay (n=55)

S. No.	Time interval / Glycemic status	N	ICU Stay		Hospital Stay	
			Mean	SD	Mean	SD
1.	At admission					
	Normoglycemic	25	1.80	0.82	5.76	3.51
	Hypoglycemic	3	4.00	1.00	8.33	3.51
	Hyperglycemic	27	2.93	1.24	9.33	3.03
	Statistical sig. (ANOVA)		F=10.72; p<0.001		F=10.62; p<0.001	
2.	At 12 hr					
	Normoglycemic	25	1.75	0.74	6.00	2.55
	Hypoglycemic	3	4.33	0.58	7.00	4.36
	Hyperglycemic	27	2.89	1.23	9.14	3.10
	Statistical sig. (ANOVA)		F=13.45; p<0.001		F=7.50; p<0.001	
3.	At 24 hr					
	Normoglycemic	26	1.88	0.95	6.46	3.13
	Hypoglycemic	2	4.50	0.71	4.50	0.71
	Hyperglycemic	27	2.89	1.19	9.04	2.93
	Statistical sig. (ANOVA)		F=9.51; p<0.001		F=6.03; p=0.004	

*Expired and LAMA patients were excluded from assessment

ICU stay duration was lower in normoglycemic as compared to hypoglycemic and hyperglycemic patients for all the three assessments as well as for overall glycemic status during 24-hr. The association was significant statistically too (p<0.001). Similar trend was also observed for hospital stay for admission and 12 hr glycemic status (p<0.001). However, at 24 hr, duration of hospital stay was minimum among those with hypoglycemia followed by normoglycemia and hyperglycemia respectively (p=0.004).

Discussion

The present study was carried out with an aim to study the relationship between plasma glucose level and morbidity and mortality outcome in PICU patients. For this purpose, a total of 90 critically ill children aged <15 years admitted to PICU of our facility were enrolled in the study. Age of children enrolled in the study ranged from 2 months to 15 years with a mean age of 5.28±5.56 years. Male to female ratio was 1.57. Haque and Bano [14] in another study reported the mean age of PICU patients to be 2 years only but reported a male-to-female ratio 1.94, which is close to ours.

The present study found respiratory system abnormalities (n=30; 33.3%), central nervous system abnormalities (n=15; 16.7%), infections (n=11; 12.2%) and cardiovascular abnormalities (n=9; 10%) as the dominant etiologies. Renal etiology and Poisoning were least common found in 1 (1.1%) case each. The etiological profile of PICU patients in different case series has shown a considerable variability. However, in most of the series, respiratory illnesses have

shown a dominant role but with variable proportions. Volakli *et al*. [15] in their series also reported respiratory illness as the most dominant cause of PICU admission (22.3%). However, Begum *et al*. [16] in a recent study from Telangana reported neurological (27.8%) etiology as the most common followed by respiratory (25.6%) etiology. In general, most of the studies conducted in PICU have shown respiratory, cardiovascular, gastrointestinal and CNS abnormalities to comprise the majority of study population.

In present study, almost half the patients were discharged after recovery (n=44; 48.7%) while 28 (31.1%) expired during the treatment. Out of 90 cases 7 (7.8%) cases left against medical advice and 11 (12.2%) were referred to higher facility for further treatment. Compared to present study, workers like Khilnani [17], Volakli *et al* [15], reported much lower mortality rate (<10% mortality rate), The mortality rate in present study was comparable to that reported by Das *et al*. [18] and Bhutia *et al*. [19] who reported it to be 27.34% and 35.29% respectively. The extreme variability in mortality rates in different studies could also be owing to difference in underlying etiology and other risk factors.

In present study, duration of ICU stay ranged from 1 to 8 days with a mean of 3.14±1.61 days. Duration of hospital stay ranged from 2 to 14 days with a mean of 6.41±3.13 days. Khilnani *et al*. [17] in their study close to our study reported the mean duration of PICU stay as 4.52 days while Haque and Bano [14] reported it 3.2 days which is more close to the findings of present study. PICU stay duration as observed in present study was in consonance with most of the contemporary clinical studies.

In present study, a total of 35 (38.9%) patients required mechanical ventilation. Mechanical ventilation need has been reported to vary from 8.5% to 90% [14, 15, 17, 19] in different studies. The mechanical ventilation rate in present study was in agreement with that reported by Khan *et al*. [20] who reported it in 37.5% of their cases.

In present study, a significant association was observed between mean plasma glucose levels and outcome. Mean plasma glucose levels were maximum for those who expired and minimum for those who were referred to higher facility. Mean plasma glucose levels were in between these two extremes for those who were discharged after recovery. On evaluating the association between outcome and glycemic status (normoglycemic, hypoglycemic and hyperglycemic) at different time intervals, majority of normoglycemic and hyperglycemic patients were either discharged after recovery or were referred to higher facility while majority of hypoglycemic patients expired. Similarly, mechanical ventilation need was also found to be significantly associated with deranged glycemic status. Both ICU stay as well as hospital stay duration in general were significantly lower in normoglycemic as compared to hypoglycemic and hyperglycemic patients in all the assessments.

Similar to findings of present study, Lodha *et al*. (2009) [5] also found mortality rate to be maximum among hypoglycemic (66.7%) patients and minimum among normoglycemic patients (27.1%). They reported mortality rate of 37.9% in hyperglycemic patients. In present study too, we found mortality rate to be 70% in hypoglycemic, 35.7% in hyperglycemic and only 19.4% in normoglycemic patients, thus showing that deranged glycemic levels were significantly associated with poor outcome.

The present study endorsed the findings of previous studies that report a high prevalence of glycemic variability among PICU patients which in turn have an impact on clinical course as well as outcome.

Conclusion

The present study was carried out to evaluate the effect of plasma glucose levels within 24 hours after admission on the outcome among children admitted to pediatric intensive care unit.

Three plasma glucose measurements were made at admission, 12 hours and 24 hours after admission. All the patients were followed up till outcome. Following were the highlights of the study:

1. Age of children enrolled in the study ranged from 2 months to 15 years with a mean age of 5.36±5.73 years. Majority of patients were males (61.1%).
2. On final diagnosis, respiratory system abnormalities (n=30; 33.3%), central nervous system abnormalities (n=15; 16.7%), infections (n=11; 12.2%) and cardiovascular abnormalities (n=9; 10%) were dominant etiologies. Renal etiology and Poisoning were least common found in 1 (1.1%) case each.
3. At admission, 12 hrs and 24 hrs intervals, 50%, 52.2% and 54.4% patients respectively were hyperglycemic, 36.7%, 35.6% and 34.4% respectively were normoglycemic and 13.3%, 12.2% and 11.1% were hypoglycemic.
4. Maximum number of the patients enrolled in the study were discharged after recovery (n=44; 48.7%) while 28 (31.1%) expired during the treatment. Out of 90 cases 7 (7.8%) cases left against medical advice and 11 (12.2%) were referred to higher facility for further treatment.
5. Duration of ICU stay ranged from 1 to 8 days with a mean of 3.14±1.61 days. Duration of hospital stay ranged from 2 to 14 days with a mean of 6.41±3.13 days.
6. A total of 35 (38.9%) patients required mechanical ventilation during ICU stay.
7. On evaluating the association between outcome and glycemic status (normoglycemic, hypoglycemic and hyperglycemic) at different time intervals, majority of normoglycemic and hyperglycemic patients were either discharged after recovery or were referred to higher facility while majority of hypoglycemic patients expired. Statistically, there was a significant association between glycemic status and outcome.
8. Both ICU stay as well as hospital stay duration in general were significantly lower in normoglycemic as compared to hypoglycemic and hyperglycemic patients in all the assessments.

The findings of present study thus showed that plasma glucose levels are significantly associated with PICU outcome as well as duration of PICU and hospital stay. It was also seen that plasma glucose levels were affected by the underlying etiology, however, the etiology did not affect the outcome. These findings thus suggest that plasma glucose levels can play a predictive role and can thus guide the management course of children admitted to PICU.

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