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Original research article

Association of Hyperglycemia with Clinical Outcome in Critically Ill Children : An Observational Study

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Abstract

Background: Stress induced hyperglycaemia and its effects are a fairly common cause of concern in recent times, in the ICU settings with it being linked directly to mortality and morbidity. In this prospective observational study, we tried to find the salient demographic profile in stress induced hyperglycaemia, if any. Clinical outcome and its correlation to the type of diagnosis has also studied.

Objective: To evaluate the association of hyperglycaemia with clinical outcome of critically ill children. To assess the variation in incidence of hyperglycaemia with different diagnoses of children admitted in PICU.

Material and Methods: This was a prospective observational study done in Pediatric Intensive Care Unit of a government run tertiary level hospital on 400 children in the age group between 2months to 15 years with a PEWS of 5 or more at the time of admission, over a period of one-year period between April 2018 to May 2019.

Results: Hyperglycemia was observed in 31% of study population(n=124). Hyperglycaemia was mostly observed in CNS disease (n=78, 62.9%) followed by renal disease (n=36, 29%). Most of the hyperglycemic patients had (n=56, 45.16%) BMI <-3SD. There was statistically significant association found between Glucose Level, Nutritional Status and mortality (P=0.001)**.** Many hyperglycemic patients (n=37, 29.8%) required mechanical ventilation(p=0.001). Ionotropic support given to 49(39.5%) hyperglycemic patients (P=0.001). Among total 28 deaths, 19 (67.8%) patients had persistent hyperglycaemia, 7(25%) had impaired glycaemic level. Statistically significant difference found in Mortality Rate according to glycaemic level(P=0.001).

Conclusion: Hperglycemia is a common finding in PICU which was more frequently observed in those children who needed mechanical ventilation and ionotropes. It may be associated with poorer outcome in term of mortality and longer PICU LOS.

Keywords: Hperglycemia, Pediatric, Mortality, PICU

Introduction

Stress induced hyperglycaemia (SH) is quantitatively taken as a random blood glucose level more than 150 mg/dL in the setting of a critical illness and without prior evidence of diabetes mellitus[1]. Globally it is estimated that around 60% of the critically ill children present with stress hyperglycaemia[2]. Stress hyperglycaemia is thus defined as a 'transient hyperglycaemia during an acute illness, usually restricted to patients without prior evidence of diabetes, with reversion to normal after discharge[3].

Historically, it has been considered an adaptive response to stress which improved survival or was inconsequential[4]. However, recent studies have challenged this thought and has concluded SH to be harmful and a predictor of worst outcome in relation to critical care[5]. Comparatively, less is known about the effects of hyperglycaemia in PICU. It carries a negative prognosis and indicates poor neurological outcome in paediatric patients with head injury[6].

Umpierrez et al concluded that hyperglycaemia (serum glucose >126 mg/dL or >6.99 m mol/L) is a common entity among hospitalised patients and is a marker of poor clinical outcome and mortality in patients admitted in critical care units[7]. Branco et al showed relation between blood glucose level and mortality in children with septic shock and that a level >176mg/dL is associated with higher rates of mortality[8].

Material and Methods:

This study was a prospective observational study performed at the PICU of the Department of Paediatric Medicine, Gandhi Medical College, Bhopal MP. It is a tertiary care referral centre and is under the ministry of medical education of the state govt. The study population consisted of all children between 02 months to 15 years of age who were admitted in the department. The study span was a period of 1 year from April 2018 to May 2019.

Children were categorised into age-groups (2-12 months, 1-5 years, 5-10 years, 10-15 years). Critically ill patients with Paediatric Early Warning Score (PEWS) of 5 or more were considered. Children with blood glucose level <54 mg/dL at admission, known diabetics and those on any drug likely to cause hyperglycaemia were excluded. That left us with 400 patients. Outcomes were classified as either discharged successfully or left against medical advice or death. The exposure variable was the glucose category, obtained by point of care device[9] and confirmed by serum glucose from blood obtained by venepuncture. The groups were – 1. Normoglycemic (BG<150mg/dL) and 2. Hyperglycaemic (BG > or equal to 150 mg/dL). Serial readings were taken, and mean was calculated and accordingly further grouped as 1. Normal (70-110 mg/dL) 2. Impaired (111-149 mg/dL) and 3. Hyperglycaemia (> or equal to 150 mg/dL). Complete physical examination was done, and investigations were ordered. Outcome was noted at the end of length of stay (LOS) in PICU.

Informed consent was obtained for every subject. The study was cleared by the Ethical Committee and there was no conflict of interest.

Statistical Analysis

Statistical analysis was done using statistical package of Statistical Package of Social Sciences (SSPS 22, Chicago Inc., USA). The quantitative variables were compared using mean and the qualitative ones were using proportions. $P < 0.05$ was taken as the level of significance. Chi square test was used. Additionally, sensitivity and specificity along with negative and positive predictive value of hyperglycaemia with relation to outcome at PICU were also assessed.

RESULTS

Study Flow chart

Study Duration: April 2018 to May 2019

↓

Total Admissions: 7106

↓

PEWS ≥ 5: 1055

↓

Excluded: 633

↓

Enrolled: 633

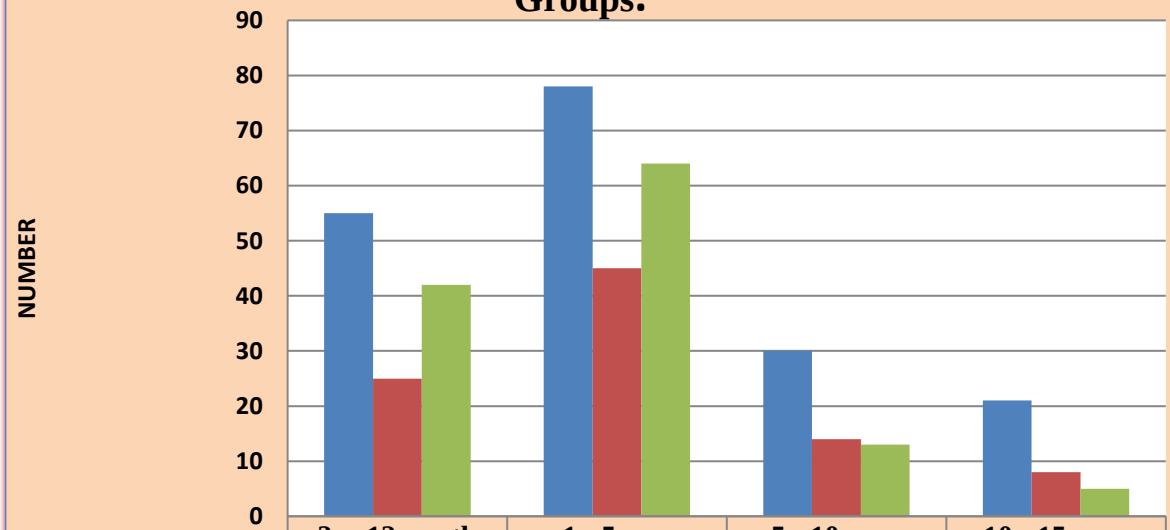
↓

LAMA: 22

↓

Total Patients on whom study was completed: 400

Figure 1: Association of Glycemic levels With Various Age Groups.



	2m-12month	1y-5year	5y-10 year	10y-15 year
Normal	55	78	30	21
Impaired	25	45	14	8
Hyperglycaemia	42	64	13	5

Figure 2: Glycemic Levels According to gender

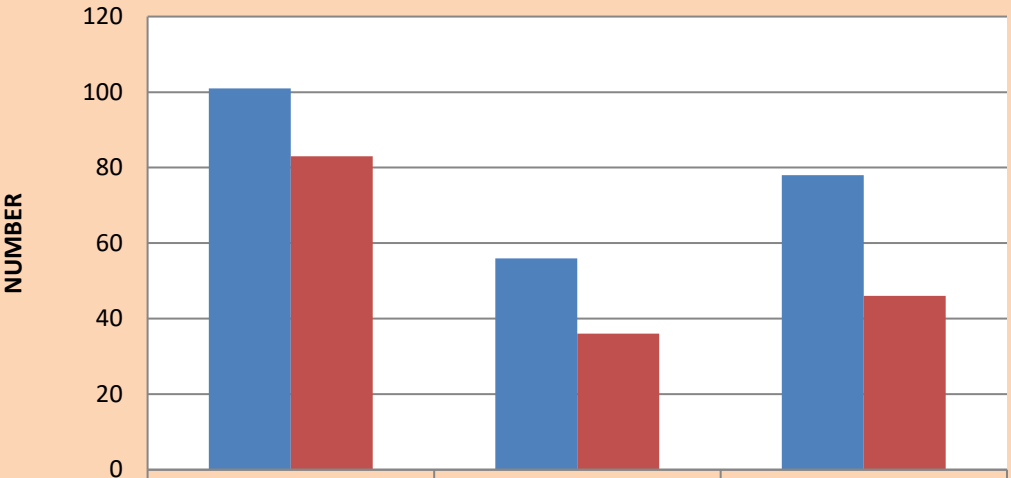


Table 1: Incidence of hyperglycaemia according to primary body system involved.

Blood glucose(mg/dl)	CNS	CVS	Renal System	Abdomen	Others	Total
70-110 (Normal)	82	25	54	21	2	184
111-149 (impaired)	31	11	42	7	1	92
>=150 (hyperglycaemia)	78	7	36	2	1	124
Total	191	43	132	30	5	400
Chi Square test value	**30.1**					
Significance 'p' Value	**0.001(HS)**					

Hyperglycaemia was seen in maximum number of CNS patients i.e. 78(62.9%) followed closely by patients with renal pathology i.e.36(29%). Statistically, highly significant association found with hyperglycaemia, in relation to the primary system involved, at the time of presentation. **(P=0.001)**

Table 2: Association of glycemic status with system involvement and mortality

Blood glucose (mg/dl)	Outcome	CNS	CVS	Renal	Abdomen	Others	Total
70-110 (Normal)	Death	2	0	1	0	1	4
	Discharge	73	30	40	27	10	180
111-149(impaired)	Death	4	1	2	1	0	8
	Discharge	48	5	22	4	5	84
>=150(hyperglycaemia)	Death	13	1	6	2	0	22
	Discharge	60	4	31	0	3	102
Chi Square test value		**38.02**					
Significance 'p' Value		**0.001(HS)**					

Test of significance observed highly statistically significant association between Glycemic Level, system involvement and mortality. (**P=0.001)**

Table 3: Association of glycaemic Level with Nutritional Status.

Blood glucose(mg/dl)	BMI <-3SD	-3SD to-2SD	-2SD to median	Median or more	Total
70-110 (Normal)	43	75	64	2	184
111-149(impaired)	14	36	41	1	92
>=150(hyperglycaemia)	56	29	37	2	124
Total	113	140	142	5	400
Chi Square test value	**30.1**				
Significance 'p' Value	**0.001(HS)**				

There was statistically significant association found between glycaemic Level &nutritional Status i.e. poorer the nutritional status, more are the chances of hyperglycaemia. (**P=0.001)**

Table 4: Association of glycemic level and nutritional status with mortality

Blood glucose(mg/dl)	Outcome	BMI <-3SD	-3SD to -2SD	-2SD to median	Median or more	Total
70-110 (Normal)	Death	1	1	2	0	4
	Discharge	48	60	71	1	180
111-149(impaired)	Death	0	5	2	1	8
	Discharge	13	32	39	0	84
>=150(hyperglycaemia)	Death	19	1	2	0	22
	Discharge	43	24	32	3	102
Chi Square test value		**44.65**				
Significance 'p' Value		**0.001(HS)**				

There was statistically significant association found between Glycemic Level, Nutritional Status and mortality. (**P=0.001)**

Table 5: Requirement of Mechanical Ventilation according to Glycaemic levels.

Blood glucose(mg/dL)	Requirement of Mechanical Ventilation	
	YES	**NO**
70-110 (Normal)	11(2.75 %)	173(43.25)
111-149(impaired)	19(4.75 %)	63(15.75)
>=150(hyperglycaemia)	37 (9.25 %)	87(21.75)
Total	**67(16.75 %)**	**333(83.25%)**
Chi Square Value	**32.3**	
Significance 'p' value	**0.001(HS)**	

More patients with hyperglycaemia require invasive ventilation at some point during their stay. Statistically significant association was found between requirement of Mechanical Ventilation and glycaemic levels. **(P=0.001)**

Table 6: Mortality Rate according to Glycaemic Level.

Blood glucose(mg/dL)	Mortality	
	YES	NO
70-110 (Normal)	2(0.5%)	182
111-149(impaired)	7(1.75%)	85
>=150(hyperglycaemia)	19(4.75%)	105
Total	28(7.0%)	372
Chi Square Value	23.1	
Significance 'p' Value	0.001(HS)	

There was statistically significant difference found in Mortality Rate according to glycaemic level. (P=0.001)

Table 7: Odds Ratio (OR) for hyperglycaemia related mortality

Risk Estimate			
Odds ratio	Value	95% Confidence Interval	
		Lower	Upper
For outcome	.247	.118	.516
Normal blood glucose	.513	.323	.812
Increased blood glucose	2.077	1.552	2.780

For raised blood glucose level and its relation to mortality at PICU, odds ratio (OR) was 2.77 with 95% confidence interval of 1.55-2.78 i.e. odds of mortality in patients of raised blood glucose is 2.077 times the odds of patients with normal blood glucose level.
The positive predictive value of hyperglycaemia (blood glucose level > 150 mg/dL) for prediction of mortality in critically ill children in PICU was 16.2% whereas negative predictive value was 95.5%. The

Discussion

The cellular injury in critical illness is a cumulative result of hypoxia, oxidative stress, systemic inflammation and/or reduced and redistributed blood flow[10]. It occurs due to mainly 2 factors increased gluconeogenesis in relation to glucose clearance and insulin resistance at the cellular level preventing glucose uptake[11]. Earlier it was considered that hyperglycaemia in the setting of a critical illness was a protective adaptive response to stress. However, newer studies have refuted this hypothesis. The present study was aimed at discerning whether hyperglycaemia was related to poor clinical outcome or was unrelated to the outcome and only a marker of acute stress associated with critical illness.

In our study, Hyperglycaemia was seen maximum (n=78) in patients with CNS involvement, followed by patients with renal involvement (n=36). There was statistically highly significant difference in incidence of hyperglycaemia according to body system involved (P=0.001). In a retrospective cohort study by Kandil SB et al (2013), majority of children presented with respiratory followed by cardiac involvement in both the groups and the difference between the groups was significant[12]. In our study Hyperglycaemic patients (>=150 mg/dl) had longest mean duration of stay of around 8 days which was statistically not significant. Hall NJ et al (2004) in their study documented median length of stay of 9.3 days. On regression analysis, they observed level of glucose to be significantly related to length of stay (P <.0001)[13].
Mechanical ventilation requirement were observed in most of the hyperglycaemic patients(n= 37, 29.8%)(p=0.001). Klein et al (2008) observed that patients with glucose levels more than

200mg/dL (> 11.1mmol/L) on the first day of PICU admission had a significantly higher mechanical ventilation time[14]. statistically significant association between requirement of Inotropes and glycaemic levels (n=49, 39.5%) (P=0.001). Patki VK et al (2014) observed a statistically significant higher inotropic support requirement (38.6% vs. 16.1) in hyperglycemics[15].

In this study, we observed a statistically significant association of outcome with glycaemic level (p=0.001).Out of total 28 death, 19 (4.75%) patients were hyperglycaemic, 7(1.75%) were with impaired glycaemic status and 2(0.5%) had normal blood glucose levels. Toro Polo LM et al (2018) in their study observed high mortality in patients with glucose levels >200mg/dL (> 11.1mmol/L) followed by those with glucose levels < 65mg/dL (3.61mmol/L)[16]. There was statistically significant association found between Glycemic Level, Nutritional Status and mortality(P=0.001).

To conclude, Hperglycemia is a frequent finding in PICU which was more frequently observed in those children who were mechanically ventilated and on ionotropic support and it may be associated with poorer outcome in term of mortality and longer PICU LOS. Further multicenter large scale studies are required to find out the role of hyperglycemia in outcome among critically ill children.

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