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Original Research Article

A DESCRIPTIVE STUDY ON CLINICAL PROFILE AND OUTCOME OF STRESS-INDUCED HYPERGLYCAEMIA IN CRITICALLY ILL CHILDREN

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Abstract

Background: Hyperglycemia in critically ill patients is a commonly observed finding, usually evident in the first 48 hours on admission to the ICU in at least 50% of the patients. The present study was performed to study the clinical profile and outcome of stress-induced hyperglycaemia (SIH) in critically ill children. **Materials and Methods:** The present study was performed on 107 critically ill children. Those children who were found to have high blood glucose (≥ 150 mg/dl) were enrolled. A thorough history regarding the etiology and risk factors was obtained, and a physical examination was done. Investigations related to the diagnosis were taken, including the complete blood count, liver function tests, renal function tests, blood cultures, urine cultures, chest X-Ray, and electrolytes. The outcome was documented as dead or discharged. **Results:** Our study reported 94%, 94% and 92% deaths with abnormal heart rate, respiratory rate and blood pressure. Of all population, 81% had prolonged capillary refill time. The total count, platelet count, blood urea, serum creatinine, liver function test (LFT), serum electrolyte, body temperature, blood culture, and chest X-ray were not correlated significantly with outcomes. However, the C-reactive proteins (CRM), oxygen support, duration of hyperglycaemia, need for mechanical ventilation and need for inotropic support were found significantly correlated with the outcomes. The sepsis was reported as the main (31%) etiology for SIH. **Conclusion:** Stress-induced hyperglycemia is commonly seen in critically ill children with unstable cardiovascular and mental status. Sepsis is the most common etiology of stress hyperglycemia.

INTRODUCTION

In critically ill patients, hyperglycemia is a commonly observed condition often evident within the first 48 hours of admission to the ICU in at least 50% of patients.[1] Numerous studies have demonstrated a significant association between blood glucose levels upon ICU admission or during the ICU stay and the severity of patient outcomes.[2-3] Stress-induced hyperglycemia (SIH) leads to insulin resistance and elevated blood glucose levels through various mechanisms.[4] Counter-regulatory hormones such as catecholamines, cortisol, glucagon, and growth hormone disrupt glucose homeostasis. At the same time, an increase in inflammatory cytokines further exacerbates the metabolic environment.[4] As a result, hepatic gluconeogenesis becomes uncontrolled, and the glucose uptake by skeletal muscle through the glucose transporter type 4 (GLUT-4) is impaired.[4] Moreover, insulin levels themselves are insufficient to counteract the state of hyperglycemia.[5]

Hyperglycemia, defined as blood glucose levels exceeding 180 mg/dl, has been associated with increased mortality in a retrospective study conducted in the USA, underscoring the importance of stringent glycemic control.[6] Furthermore, studies have highlighted that it is stress-induced hyperglycemia (SIH) rather than diabetic hyperglycemia (DH) that primarily contributes to elevated mortality and morbidity rates.[7] Achieving proper glycemic control in the inpatient setting necessitates a coordinated approach involving a multidisciplinary team.[8] This process involves accurate diagnosis, optimal management within the ICU, and seamless continuity of care, which significantly aids in reducing morbidity risks.[9]

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Intravenous insulin therapy has traditionally been the standard treatment for hyperglycemia.[10] Recently, continuous glucose monitoring (CGM) systems have been introduced in hospitals. These devices allow for continuous glucose monitoring with minimal reliance on healthcare professionals.[10,11] Although there is no definitive evidence of improved patient outcomes, CGM has substantially reduced the risk of hypoglycemic episodes.[12] Increased blood glucose variability and a higher frequency of hypoglycemic events are also recognized as contributors to poor outcomes.[13]

Only a few studies have evaluated the association between clinical profile and SIH in children. Hence the present study was performed to study the clinical profile of critically ill children and its association with the outcome of SIH.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at the Intensive care unit of the Paediatric Department, GMKMCH, Salem, for one year, on 107 children. Informed consent for participating in the study and Institutional ethical committee clearance was obtained before the start of the study.

Inclusion Criteria

All children above one month to 12 years of age who were admitted to the paediatric intensive care unit with blood glucose ≥ 150 mg/dl were included.

Exclusion Criteria

All Children who are known cases of Type I Diabetes and with long-term steroid therapy and patients who refused to participate and ageing > 12 years were excluded.

Methodology

Blood glucose was checked for all the critically ill children admitted to the paediatric ICU. Those children were enrolled based on inclusion and exclusion criteria after getting consent from their parents. A thorough history regarding the etiology and risk factors was obtained, and a physical examination was done. Investigations related to the diagnosis were taken, including the complete blood count, liver function tests, renal function tests, blood cultures, urine cultures, chest X-Ray and electrolytes. All these data were entered in the proforma, and treatment was given according to standard guidelines. The outcome was documented as Dead or Discharged.

Parameters normal range

Variables	Normal range
Total count:	4000 – 12000
Platelet count	1.5 – 4 lakhs
Creatinine	0.03 – 0.59 mg/dl
Urea	7 – 18 mg /dl
Total bilirubin	< 1 mg /dl
SGOT	15 – 50U/L
SGPT	5 – 45 U/L
Sodium	135 – 145 mmol /dl
Potassium	3.5 -4.5 mmol/l
CRP	<6 mg/l
Blood culture	As defined by the cultural positivity
Chest x-ray	Abnormal X-ray findings as defined by a radiologist

Statistical Analysis

The data was gathered and entered into MS Excel. Frequency means percentages, standard deviations, chi-square coefficients of correlation, and p-values were determined using the SPSS-18 software. The significance of a difference between two quantitative variables was calculated using the Chi-square test, and a p-value of < 0.05 was considered significant.

RESULTS

Among 107 patients, 61 (57%) male patients were more than female 46 (43%). The mortality reported was found to be comparable in both genders. 48 (45%) were < 1 year, and mortality was also highest at 21 (41%) in this age group. 70 (65%) had a fever; of the total deaths, 34 (67%) had a fever. Breathlessness, acute loss of consciousness (ACLOC), vomiting, seizure and loose stools were reported in 62 (58%), 57 (53%), 21 (20%), 40 (37%) and 16 (15%), respectively.

33 (31 %) had a positive family history of diabetes, and 74 (69 %) did not have a family history of diabetes. Of all subjects reported with a family history of diabetes, death was found in 16 (31%) patients. Of the total deaths, at initial presentation, 2 (4%) were alert, 10 (20%) were verbally responsive, 29 (56%) were pain responsive, and 10 (20%) were unresponsive. The AVPU scale was found to be statistically significant ($p<0.05$) (Table 1).

A total of 48 (94%), 48 (94%) and 47 (92%) death was reported with abnormal heart rate, respiratory rate and abnormal blood pressure, and the effect was statistically significant ($p<0.05$) between normal and abnormal parameters. 86 (81%) had prolonged capillary refill time, and the body temperature and hyperglycaemia did not correlate significantly with the outcome (Table 2).

Of the total deaths, 39 (36%) were in the population who had prolonged hyperglycemia > 48 hours. The duration of hyperglycaemia significantly ($p<0.05$) correlated with the outcome. Whereas total count, platelet count, blood urea, serum creatinine, liver function test (LFT), serum electrolyte, blood culture, and chest X-ray were not correlated significantly with outcomes. However, the C-reactive proteins (CRM), oxygen support, need for mechanical ventilation and need for inotropic support significantly correlated with the outcomes (Table 2).

Among children presented with SIH, 31% had sepsis, 15% had a seizure disorder, 13% had acute-CNS infections, 13% had acute febrile illness, and 30% had other etiologies. Of all children presented with sepsis, 57% expired; with seizure disorder, 75% expired; with acute CNS infection and acute febrile illness, 50% expired. Etiological risk factors thus had a significant ($p<0.05$) correlation with the outcome (Table 3).

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Table 1: Observation of demographic data

Parameters	Outcome N (%)		P-value
	Death	Discharge	
Gender			
Male	26(51%)	35(62.5%)	0.229
Female	25(49%)	21(37.5%)	
Age group (years)			
< 1	21(41%)	27(48%)	0.187
1-5	19(37%)	24(43%)	
> 5	11(22%)	5(9%)	
Fever			
Present	34(67%)	36(64%)	0.796
Absent	17(33%)	20(36%)	
Breathlessness			
Present	26(51%)	36(65%)	0.164
Absent	25(49%)	20(35%)	
Acute loss of consciousness (ALOC)			
Present	47(92%)	10(18%)	0.001
Absent	4(8%)	46(82%)	
Vomiting			
Present	12(23.5%)	9(16%)	0.332
Absent	39(76.5%)	47(84%)	
Seizures			
Present	22(53%)	18(32%)	0.24
Absent	29(57%)	38(68%)	
Loose stools			
Present	12(23.5%)	4(7%)	0.014
Absent	39(76.5%)	52(93%)	
Family history of diabetes			
Present	16(31%)	17(30%)	0.91
Absent	35(69%)	39(70%)	
AVPU			
Alert	2(4%)	17(30%)	0.003
Verbal responsive	10(20%)	24(43%)	
Pain responsive	29(56%)	12(21%)	
Unresponsive	10(20%)	3(5%)	

Table 2: Observation of laboratory test results of all subjects

Parameters	Outcome N (%)		P-value
	Death	Discharge	
Total count			
High	26(51%)	25(45%)	0.752
Low	5(10%)	5(9%)	
Normal	20(39%)	26(46%)	
Platelet count			
High	1(2%)	2(3.5%)	0.856
Low	14(27.5%)	14(25%)	
Normal	36(70.5%)	40(71.5%)	
Blood urea			
High	19(37%)	14(25%)	0.17
Normal	32(63%)	42(75%)	
Serum creatinine			
High	11(21%)	6(10%)	0.127
Normal	40(79%)	50(90%)	
Liver function test (LFT)			
High	10(20%)	7(12.5%)	0.315
Normal	41(80%)	49(87.5%)	
Serum electrolytes			
High	14(27.5%)	11(20%)	0.34
Normal	37(72.5%)	45(80%)	
C- reactive protein (CRM)			
Positive	37(72.5%)	20(35.5%)	0.001
Negative	14(27.5%)	36(64.5%)	
Blood culture			
Growth	17(33%)	10(18%)	0.066
No growth	34(67%)	46(82%)	
Chest x-ray			
Abnormal	22(43%)	19(34%)	0.328
Normal	29(57%)	37(66%)	
Oxygen support			
Yes	51(100%)	51(91%)	0.029
No	0	5(9%)	

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Mechanical ventilation			
Yes	51(100%)	13(23%)	0.001
No	0	43(77%)	
Inotropes support			
Yes	51(100%)	21(37.5%)	0.001
No	0	35(62.5%)	

Table 3: Observation of etiological risk factors in patients

Etiology	Outcome N (%)		P-value
	Death	Discharge	
Sepsis	19(39%)	14(25%)	0.004
Seizure disorder	12(23%)	4(7%)	
Acute CNS infection	7(13.5%)	7(12.5%)	
Acute febrile illness	7(13.5%)	7(12.5%)	
Others	6(12%)	24(43%)	

DISCUSSION

SIH was previously thought to be playing a protective role in critically ill situations. But in recent years, various studies have been conducted to understand the outcome of SIH. Most of these studies has proven that SIH can cause adverse outcome in critically ill situations.[2-3] Some studies suggest that SIH can be harmful only if prolonged, whereas others say that even transient SIH can cause end-organ damage. It is important to know the effects of SIH and understand whether or not it is an individual risk factor causing mortality in critically ill children so that measures can be taken to overcome its effects and, thereby, the outcome can be improved.[4-5]

In this study, most (45%) children with stress hyperglycemia were infants <1 year of age. A total of 40% of the study population belonged to the 1-5 years age group. Only 15% of children with stress hyperglycemia were > 5 years of age. Thus, it was noted that the infantile age group suffered more from stress hyperglycemia, and as age progressed, the incidence of stress hyperglycemia was less. These findings in the present study follow earlier reported studies.[14]

It was also seen that in this study, 57% were male, and only 43% were females. Similarly, a study conducted by Weiss et al. also showed male predominance. In the present study, the incidence differed in various age groups and among different sex. The outcome of stress hyperglycemia in terms of mortality in various age groups and sex was not significant statistically.[15]

Only 31% of this study's participants had a family history of diabetes, whereas 69% did not. And just 31% of all deaths had a history of diabetes in the family. It should be mentioned that the current study found no relationship between a family history of diabetes and either the frequency or severity of stress hyperglycemia. Similar research by Shehadeh et al., which revealed no link between the incidence of stress hyperglycemia and a family history of diabetes, is analogous to this one.[16] However, Graham et al. study from 2002 in Canada discovered a connection between stress hyperglycemia and a family history of diabetes.[17]

Out of 107 study population, 57 had an acute loss of consciousness (53%), and of the total deaths, 92% were in ALOC at presentation. Of the total children who were alert at admission, 10% expired. Similarly, among children who responded verbally, 29% expired. Among those who responded to painful stimuli, 70% expired. 76% of the unresponsive children had expired. So it was noted that children with SIH and ALOC at presentation had a very poor prognosis and that the death rate increased with a drop in the level of consciousness in the AVPU scale. These findings in the present study are consistence with the results of Plummer et al. investigations.[18]

This study also revealed that the cardiovascular status of critically ill children at admission with SIH correlated significantly with the outcome. A vast majority of the children with SIH had abnormal heart rates (83%), low blood pressure (82%), and prolonged capillary refill time (81%). Of the total deaths, 94 % had tachycardia, 92% had hypotension, and 92% had prolonged CRT. Also, 92 % of the study group had abnormal respiratory rates, and 94% of the total deaths had tachypnoea. Thus, SIH was highly associated with abnormal cardiorespiratory status, and the outcome was markedly poor in children with abnormal cardiorespiratory status manifesting with SIH. Our findings were consistence with the findings of Rajpurohit et al., who also reported a significant correlation of acute myocardial infarction (AMI) with SIH.[19] The study showed an elevated incidence of complications such as arrhythmias, cardiogenic shock, progression to severe heart failure, and a significant increase in mortality. Hence, SIH in patients with MI had a critical role in the outcome.

Among children whose transient SIH resolved within 6 hours, 23.5% expired. Similarly, among those children in whom SIH lasted for 24 hours and 24-48 hours, the percentage of deaths was 36% and 78%, respectively. Notably, 90% of children with prolonged SIH lasting more than 48 hours expired. Thus, this study revealed the relationship between SIH duration and the mortality rate. The duration of hyperglycemia was longer in non-survivors (71%, 14% of PICU days) than in survivors (37%, 5% of PICU days, p .001), and the peak hyperglycemia, duration, and intensity of hyperglycemia were each

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individually associated with mortality ($p<0.05$) in the study by Srinivasan et al. Thus, they came to the independent relationship between peak blood glucose and its duration and mortality (p .05) as their study's conclusion.[20]

This study found no relationship between laboratory results such as total count, platelet count, renal function tests, liver function tests, serum electrolytes, and blood culture with SIH. There were two exceptions, CRP and chest X-ray, favourably connected with the outcome. Some earlier studies also reported an insignificant correlation of laboratory results with SIH.[21]

In this study, of the total children with stress hyperglycemia, 95.5% had some form of oxygen requirement, and 60% needed mechanical ventilation. A total of 67% of the children needed inotropic support. Each child (100%) who died was mechanically ventilated and under inotropic support at some point during the illness. Thus the need for intensive interventions like mechanical ventilation and inotropic support in children with stress hyperglycemia has got poor outcomes. Similarly, a study conducted by Patki et al. showed that the need for a ventilator, inotrope and length of hospital stay increased with stress hyperglycemia with a P value of 0.05.[22]

The etiological profile of this study showed that out of 107 children who presented with stress hyperglycemia, 33 (31%) cases constituted sepsis. Among these, 19 cases (57%) expired. Of the children who presented with seizure disorder (15%), 75% expired. 13% of the children presented with Acute CNS infection and acute febrile illness individually, of which 50% expired in each group. These were the four common etiologies that presented with SIH. A study by Branco et al. revealed that elevated glucose levels are a reliable predictor of mortality in septic children, with a sensitivity of 0.714, specificity of 0.724, and relative risk of 2.59. In their prospective investigation, Branco et al. concluded that elevated blood glucose is frequently linked to paediatric septic shock.[23]

All other etiologies like acute encephalopathy, ADEM, febrile seizures, trauma, neurosurgery post-operative children, envenomation, poisoning etc., with SIH contributed 28% of which 20 % expired. Of the deaths, 39% were due to sepsis, and 23%weres due to seizure disorder. Yet seizure disorder manifesting SIH had a maximum death rate (75%). So, in this study, sepsis was a common cause of SIH, but seizure disorder has higher mortality than stress hyperglycemia. This is consistent with the association between sepsis and hypoglycemia noted by Vriesendorp et al. and Branco et al.

CONCLUSION

Stress-induced hyperglycemia is commonly seen in critically ill children with unstable cardiovascular and mental status. Sepsis is the most common etiology of stress hyperglycemia. Stress hyperglycemia has got poor outcomes, especially when the duration of hyperglycemia is more than 48 hours, in an altered level of consciousness, in cases of poor cardio-respiratory status and when there is a need for intensive interventions like mechanical ventilation or inotropic support.

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