Original Research Article

Stress hyperglycemia: clinical profile and outcome in critically ill children

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ABSTRACT

Background: Stress hyperglycemia (SH) occurs commonly during critical illness in children with previously normal glucose homeostasis. Objective of present study was to study the clinical presentation, underlying illness and the outcome of stress hyperglycemia among critically ill children.

Methods: Children attending the outpatient department and the casualty were admitted to Emergency department based on the triage guidelines. Children with blood glucose above 200 mg/dl on admission to the emergency department were considered to have hyperglycemia and were shifted to the Paediatric intensive care unit or the paediatric wards for further management. Data was collected as per the proforma. The blood sugar values were followed up in these children until restoration of normoglycemia. All the children were followed up till discharge or death in case of mortality. Associated risk factors were analysed between the survivors and nonsurvivors.

Results: Among 102 children included in the study group from 1 month to 12 yrs, 55 were infants, 37 in the age group of 1-5 yrs and 10 were more than 5 yrs. 60 were males and 42 were females. Family history of diabetes was encountered in 10 children. Out of 102 children, 60 recovered to hospital discharge. Sepsis, seizures, bronchopneumonia and CNS infections were the common illness among children with stress hyperglycemia. Age less than 1 year, breathlessness, fever, shock, seizures and altered sensorium were identified to be significantly associated with mortality in children with stress hyperglycemia by univariate analysis in this study. Regression analysis revealed age less than one year, presence of lung infiltrates, longer duration of hyperglycemia, and need for Paediatric Intensive Care Unit (PICU) admission to be significantly associated with mortality. Non survivors had persistent hyperglycemia up to 48 hours in comparison to survivors. Overall mortality in the study group was 41%.

Conclusions: Incidence of stress hyperglycemia is high in infants. Infections were the common underlying diagnosis in stress hyperglycemia. Being an infant, prolonged hyperglycemia for 48 hrs and need for PICU care were significantly associated with mortality. Overall mortality in children with stress hyperglycemia is 41%.

Keywords: Critically ill children, Mortality, Stress hyperglycemia

INTRODUCTION

Stress hyperglycemia (SH) occurs commonly during critical illness in children with previously normal glucose homeostasis.¹⁻⁴ It is often discovered incidentally when

routine blood sugar measurements reveal an elevated blood glucose. It is estimated that 49-70% of children with stress hyperglycemia have BG concentrations >150 mg/dl, 20-35% of children have BG > 200 mg/dl.¹⁻⁴ However the occurrence of blood glucose more than 150

mg/dl has been reported to occur in 3-5% of the kids in the emergency room when compared with survivors, non survivors have high Blood glucose concentrates and they tend to have been exposed to longer duration of stress hyperglycemia.^{5,6}

A unique feature of critical illness is disturbed glucose homeostasis. Hence normalizing the physiological disturbance might hasten recovery. Stress hyperglycemia is a fight or flight response. There is no clear evidence on whether stress hyperglycemia is related only to the disease severity or an independent risk factor leading to mortality and morbidity.

METHODS

This is a hospital based descriptive study. Study was conducted from February 2013 to August 2014. Children between 1 month and 12 years were recruited for the study.

Inclusion criteria

All children with stress hyperglycemia diagnosed at the emergency room of the Institute were recruited.

Exclusion criteria

Children with known diabetes mellitus and those diagnosed to have diabetes or diabetic ketoacidosis during this admission were excluded. Children on long term steroids, and chemotherapy were excluded.

Children attending the outpatient department (OPD) were triaged to Emergency room as per OPD triage guidelines. Children with life threatening events, shock, respiratory distress, altered sensorium, history suggestive of poisoning, bites and injuries were considered as critically ill children. These children were triaged to be treated in emergency department (ED) of the institute at arrival.

All the children treated at ED underwent immediate capillary blood glucose estimation by finger prick method. Capillary blood glucose value of 200mg/dl and above was considered as hyperglycemia for the purpose of this study and these children were enrolled in the study.

Following stabilization at the ED children were shifted to the PICU or the medical wards as per the hospital protocol. Children who were hemodynamically stable and recovered from apparent life threatening illness were shifted to the medical units. Children with altered sensorium, respiratory distress, shock or cardio respiratory compromise required PICU care.

A detailed history was obtained from the care givers to ascertain the clinical symptoms. The vital signs including the mental status at admission to ED were recorded. Study parameters included age, gender, clinical

symptoms, vital signs at admission, frequent blood glucose estimation, family history of diabetes, lab investigations including urea, creatinine, electrolytes, total counts, sepsis workup.

Standard definitions as per Paediatric advanced life support were used for heart rate, respiratory rate, blood pressure and sensorium assessment using AVPU (A-alert, V-Verbal, P-Pain responsive, U-Unresponsive) scale. Children were evaluated for sepsis, other metabolic parameters as needed by the clinical presentation. Children underwent repeated blood glucose estimation every 6 hours until restoration of normoglycemia. The duration of hyperglycemia was noted.

Final diagnosis was arrived as bronchopeumonia, acute CNS infection, sepsis, UTI, encephalopathy, status epilepticus etc based on the clinical presentation and laboratory evidence. The data was analyzed using Epi INFO statistical software. Comparison of the study parameters were undertaken between the survivors and those who did not survive. Significant factors were subjected for multivariate analysis by regression to look for the statistical significance. The study was approved by the institutional ethics committee and the children were recruited after informed written consent from the caregivers.

RESULTS

Among 102 children with hyperglycemia, 55 children were infants and 37 were 1-5 yrs and 10 children >5yrs of age. Of 102 children, 60 were males and 42 were females. 92% denied history of diabetes in the family. 78% presented with altered sensorium, 70% with fever, 51% with breathlessness, 35% with seizures. 40% of children were unresponsive at admission.

87% had abnormal heart rate and 91% had abnormal respiratory rate. 55% of the study group were treated at the PICU. The duration of hyperglycemia was less than 6 hours in 60%. 25% of them had hyperglycemia for up to 24 hours. Underlying final diagnosis among those with hyperglycemia were sepsis, status epilepticus, bronchopneumonia, acute CNS infections, febrile encephalopathy, febrile status, intra cranial bleed, kerosene ingestion, febrile seizures, ALTB, diarrhea, reactive airway disease, bronchiolitis, scorpion sting and congenital heart disease.

No mortality was seen in those with kerosene ingestion, febrile seizures, ALTB, reactive airway disease, diarrhea, poisoning, bronchiolitis and scorpion envenomation. Higher mortality was encountered in stress hyperglycemia with sepsis, bronchopneumonia and intracranial bleed. Overall mortality was 41%. Age less than 1 year, breathlessness, fever, shock, seizures and altered sensorium were found to be significantly associated with mortality in children with stress hyperglycemia by univariate analysis in this study.

Regression analysis revealed age less than 1 yr, presence of lung infiltrates, longer duration of hyperglycemia and need for paediatric intensive care unit admission to be significantly associated with mortality. Other study parameters have been summarized in Tables 1 and 2. Significant factors shown in tables 1 and 2 were

subjected to multivariate regression analysis. Age <1 year, hyperglycemia more than 48 hours, need for pediatric intensive care unit and presence of lung infiltrates were found to be significantly associated with mortality in stress hyperglycemia.

Table 1: Comparison of the history related data in study group.

Variable	Discharge	Death	P value	Significance
Age <1 yr	22	33	0.001	S
Gender (male)	34	26	0.597	NS
F/H/O DM	54	38	0.937	NS
Fever	37	33	0.070	NS
Breathlessness	20	31	0.001	S
Seizures	33	34	0.007	S
Fit >24hrs	1	4	0.001	S
ALOC	38	40	0.001	S
Vomiting	48	37	0.280	NS
Loose stools	54	40	0.333	NS

Table 2: Comparison of the clinical parameters among the study group.

Parameter	Discharge	Death	P value	significant
Tachycardia	48	38	0.104	NS
Tachypnea	29	28	0.178	NS
Hypotension	7	14	0.006	S
Hypothermia	1	5	0.003	S
CRT >2sec	18	32	0.001	S
Pain responsive/unresponsive	38	35	0.044	S
Low total count	1	4	0.001	S
Low platelets	0	8	0.001	S
Sepsis	0	3	0.036	S
UTI	1	4	0.070	NS
Bronchopneumonia	11	17	0.014	S
Raised Urea	2	17	0.001	S
Raised Creatinine	0	16	0.001	S
Increased SGOT	0	6	0.0035	S
Hypokalemia	3	12	0.001	S
Hyponatremia	0	6	0.001	S
Low bicarbonate	3	9	0.011	S
Hyperglycemia >48 hours	0	16	0.001	S
Need for PICU care	16	39	0.001	S

DISCUSSION

Hyperglycemia in critically sick children is known to be a stress response. This is thought to be adaptive in critically ill and injured patients and is a component of the “fight or flight” response. Peripheral insulin resistance, relative insulin deficiency, impaired glucose metabolism, other medications like catecholamines may be the contributory factors for stress hyperglycemia.¹⁻⁴ This was considered to have a beneficial effect by providing a ready source of fuel for the brain, skeletal muscle, heart and other vital organs at a time of increased metabolic demand.⁷ But

recent studies in children proved the occurrence of stress hyperglycemia to have a poor outcome.⁸ Literature have shown a negative correlation of hyperglycemia with survival in pediatric ICUs.⁹ Stress hyperglycemia has been associated with increased complications, prolonged ICU and hospital stay and increased mortality.⁷ Hence most of the pediatric critical care physicians would care to avoid stress hyperglycemia but worry about the hypoglycemia encountered while attempting for a tight glycemic control.^{10,11} Mechanical ventilation, vasoactive infusions, renal replacement therapies, cardiopulmonary bypass and extracorporeal life support, therapeutic

hypothermia, prolonged immobility, nutrition support practices, and the use of medications are all known to mediate development of SH in critical illness.¹²

In this study 58 % were females and 42% were males. Studies have shown similar female preponderance of about 63%.¹³ Mean age in this study was 2 and standard deviation was 4.6. Mean age has been documented as 8.8 years in existing studies in children.¹³

Stress hyperglycemia was associated with altered sensorium, breathlessness, fever and seizures in this study. The most common diagnosis among the children with stress hyperglycemia were seizures, sepsis and bronchopneumonia. Disease specific mortality was highest among children with congenital heart disease (100%) followed by sepsis (83%) and bronchopneumonia (40%). Among the children with seizures mortality was 45% among acute CNS infections, followed by 28.5% in febrile encephalopathy and 7.4% in seizure disorder. The mortality was nil among those with febrile seizures. Studies have shown the most common diagnoses to be respiratory illness (49%), trauma (15%), and seizure (8%).¹³ 55% of children with stress hyperglycemia required intensive care treatment. Studies have shown similar results elsewhere ie., 60%.¹³

Studies have identified peak blood glucose and the duration of hyperglycemia to be risk factors for mortality.¹⁴ Studies from India has identified that hyperglycemia defined as blood glucose >180mg/dl to be associated with increased mortality. They have also identified hyperglycemia, hypoglycemia and glucose variability to be associated with multiple organ dysfunction.¹⁵

Management of stress hyperglycemia by tight glucose control was associated with risk of increased of hypoglycemia. Subsequently studies have documented moderate glucose control (140-180 mg/dl) to be associated with lower mortality and a lower risk of hypoglycemia when compared with tight glucose control.¹⁶

It has been identified that stress hyperglycemia in a critically ill child has more adverse consequences when compared to healthy individuals or diabetic patients.¹⁷ The glucose overload in critically ill children leads to increased glycolysis and oxidative phosphorylation and this leads to increased reactive oxygen species. This leads to cellular and organ system failure in critically ill children.

The overall mortality was 22% in studies elsewhere while it was 41% in our study.

Long term follow up of these children have not revealed increased risk for diabetes mellitus.¹³ However there are contradicting reports on the long term risk of diabetes among adults with stress hyperglycemia.^{18,19}

CONCLUSION

Among those with stress hyperglycemia infants constituted more than 50%. Fever, altered sensorium and breathlessness were commonly associated with stress hyperglycemia. Sepsis, seizures and bronchopneumonia were the common illness with stress hyperglycemia. Being an infant, hyperglycemia for more than 48 hrs and need for PICU care were significantly associated with mortality. Overall mortality in stress hyperglycemia was 41%.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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