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ORIGINAL ARTICLE

Insulin Metabolic Disorders and Pediatric Stress Hyperglycemia

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ABSTRACT:
Background: Hyperglycemia is common in acute illness, even in the absence of known prior insulin resistance or diabetes mellitus (DM). This stress hyperglycemia is due to elevated cortisol, glucagon, growth hormone, catecholamines, and various cytokines, which stimulate glycogenolysis and gluconeogenesis, resulting in a transient increase in blood glucose concentration that typically normalizes when the stress abates. **Aim of the study:** To evaluate the association between insulin metabolic disorders and pediatric stress hyperglycemia.**Materials and methods:** The present study was conducted in the Department of Pediatrics of the medical institute. For the study, we selected patients admitted in the ward of Department of Pediatrics. Blood glucose greater than 200 mg/dl was considered as hyperglycemia. Patients diagnosed with diabetes, receiving β agonist drugs or those, chronic renal or hepatic disease, or cystic fibrosis were excluded from the study. At the admission, we recorded patient's height, weight, BMI, and blood pressure. After 12 hours of fasting fading blood sugar, triglyceride, cholesterol levels and insulin levels were measured. A single dose of 1.75 g/kg of glucose was administered to the subjects and blood glucose was determined after 2 hours. **Results:** The mean age of the subjects was 10.57 years. The mean weight of the subjects was 32.87 kg, mean height is 1.28 m, mean BMI is 22.77 and mean systolic blood pressure is 107.87 mmHg. Glucose tolerance impairment was seen in 3 patients, BMI> 95th percentile was seen in 10 patients, systolic blood pressure >95th percentile was seen in 5 patients, HDL < 5th percentile was seen in 9 patients, triglycerides >95th percentile was seen in 20 patients, and insulin resistance was seen in 19 patients. **Conclusion**: We conclude that the risk of progression of stress hyperglycemia to diabetes mellitus is low; however, there is high prevalence of insulin resistance in these patients
Key words: Diabetes mellitus, hyperglycemia, insulin sensitivity, stress hyperglycemia.

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INTRODUCTION:

Hyperglycemia is common in nondiabetic critically ill patients admitted to adult and pediatric intensive care units (ICUs).[1,2] A strong association between the occurrence of hyperglycemia in critically ill patients and poor outcomes has been widely reported in children and adults, and the terms hyperglycemia of critical illness and critical illness hyperglycemia (CIH) were born.[3] Hyperglycemia is common in acute illness, even in the absence of known prior insulin resistance or diabetes mellitus (DM). This stress hyperglycemia is due to elevated cortisol, glucagon, growth hormone, catecholamines, and various cytokines, which stimulate glycogenolysis and gluconeogenesis, resulting in a transient increase in blood glucose concentration that typically normalizes when the stress abates.[4] Relative insulin deficiency, peripheral insulin resistance, and dehydration causing decreased renal perfusion with limitation of urinary glucose excretion may also contribute, as can certain medications. Incidences of stress-induced hyperglycemia, defined as plasma glucose levels exceeding 200 mg/mL in patients, have been documented for more than 100 years in patients experiencing severe trauma or injury.[5] Although hyperglycemia is believed to be an adaptive stress response, long-term stress-induced hyperglycemia is linked to poor clinical outcomes and increased risk of mortality. The underlying causes of hyperglycemia during critical illness are attributed to the increased hepatic glucose production and impaired glucose consumption by peripheral tissues as well as insufficient pancreatic insulin production.[6] Hence, the present study was conducted to evaluate the association between insulin metabolic disorders and pediatric stress hyperglycemia.

MATERIALS AND METHODS:

The present study was conducted in the Department of Pediatrics of the medical institute. The study was approved from the institutional ethical board prior to commencement of the study. For the study, we selected patients admitted in the ward of Department of Pediatrics. Blood glucose greater than 200 mg/dl was considered as hyperglycemia. Patients diagnosed with diabetes, receiving β agonist drugs or those, chronic renal or hepatic disease, or cystic fibrosis were excluded from the study. A written informed consent

was obtained from the subject's parents or guardians. At the admission, we recorded patient's height, weight, BMI, and blood pressure. After 12 hours of fasting fading blood sugar, triglyceride, cholesterol levels and insulin levels were measured. A single dose of 1.75 g/kg of glucose was administered to the subjects and blood glucose was determined after 2 hours. The insulin sensitivity was determined using HOMA_IR index. Metabolic syndrome was defined as presence of 3 of the followings: 1. BMI > 2SDS, 2. TG > 2 SDS, 3. HDL < 2 SDS, 4. blood pressure > 2SDS, and 5. FBS > 100. According to American Diabetes Association guidelines, diabetes was defined as FBS>126 mg/dl or BS > 200 mg /dl after 2 hours in glucose tolerance test. FBS 100- 125 and BS 2 hour after OGTT 140 -199 were considered as pre diabetes state.

The statistical analysis of the data was done using SPSS version 11.0 for windows. Chi-square and Student's t-test were used for checking the significance of the data. A p-value of 0.05 and lesser was defined to be statistical significant.

RESULTS:

Table 1 shows the demographic data of the subjects. The mean age of the subjects was 10.57 years. The mean weight of the subjects was 32.87 kg, mean height is 1.28 m, mean BMI is 22.77 and mean systolic blood pressure is 107.87 mmHg. Table 2 shows the metabolic profile of the patients. Glucose tolerance impairment was seen in 3 patients, BMI> 95th percentile was seen in 10 patients, systolic blood pressure >95th percentile was seen in 5 patients, HDL < 5th percentile was seen in 9 patients, triglycerides >95th percentile was seen in 20 patients, and insulin resistance was seen in 19 patients. The most prevalent component of metabolic syndrome in our study is dyslipidemia. 28 patients had dyslipidemia. 20 of them had hypertriglyceridemia and 9 had low HDL levels. No patient was seen to have developed type I diabetes mellitus as per guidelines. [Fig 1]

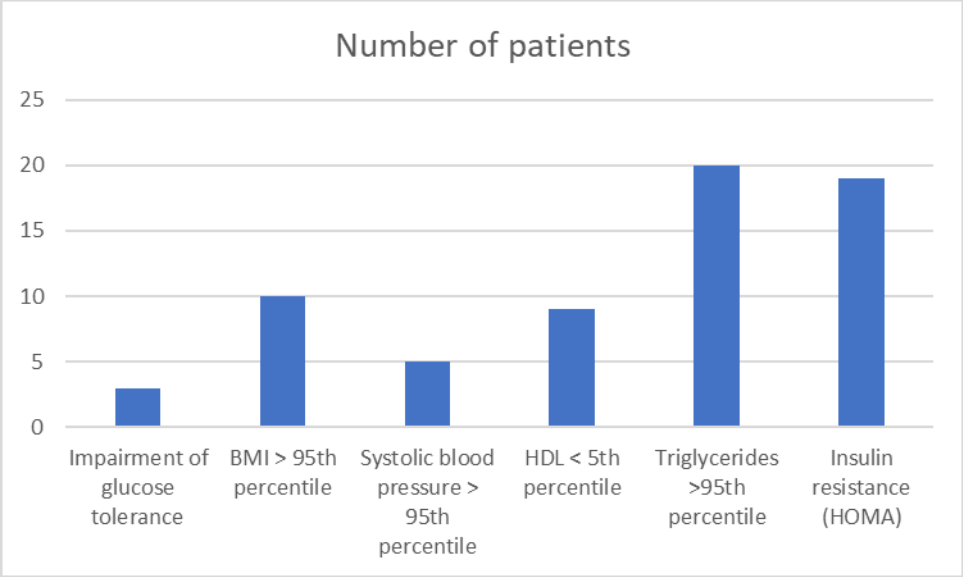
Table 1: Demographic data

Variables	Mean value
Age (years)	10.57
Weight (kg)	32.87
Height (m)	1.28
BMI	22.77
Systolic blood pressure (mmHg)	107.87

Table 2: Metabolic profile of the patients

Variables	Number of patients
Impairment of glucose tolerance	3
BMI > 95th percentile	10
Systolic blood pressure > 95th percentile	5
HDL < 5th percentile	9
Triglycerides >95th percentile	20
Insulin resistance (HOMA)	19

Figure 1: Metabolic profile



DISCUSSION:

The present study was conducted to evaluate the association between insulin metabolic disorders and pediatric stress hyperglycemia. A total of 100 patients with history of hyperglycemia were selected for the study. The most prevalent component of metabolic syndrome in our study is dyslipidemia. 28 patients had dyslipidemia. 20 of them had hypertriglyceridemia and 9 had low HDL levels. No patient was seen to have developed type I diabetes mellitus as per guidelines. The results were compared to previous studies from the literature. Wintergerst KA et al evaluated retrospectively plasma glucose levels and the degree of hypoglycemia, hyperglycemia, and glucose variability in a PICU. Patients in the highest maximal glucose quintile had a significantly longer median PICU length of stay, compared with those in the lowest quintile (7.5 days vs 1 day). Mortality rates increased as patients' maximal glucose levels increased, reaching 15.2% among patients with the greatest degree of hyperglycemia. Hypoglycemia was also prevalent, with 18.6% of patients (182 of 980 patients) having minimal glucose levels of < or = 65 mg/dL. There was an increased median PICU length of stay (9.5 days vs 1 day) associated with glucose values in the lowest minimal quintile, compared with those in the highest quintile. Hypoglycemia was correlated with mortality rates; 16.5% of patients with glucose levels of < or = 65 mg/dL died. Glucose variability also was associated with increased length of stay and mortality rates. In multivariate logistic regression analyses, glucose variability, taken with hyperglycemia and hypoglycemia, showed the strongest association with mortality rates. It was concluded that hypoglycemia, hyperglycemia, and, in particular, increased glucose variability were associated with increased morbidity (length of stay) and mortality rates. Wu Y et al investigated the incidence of hyperglycemia of patients in the pediatric intensive care unit (PICU) after receiving abdominal surgery and its association with clinical outcomes. A total of 193 children met the inclusion criteria of our research. Maximum glucose levels ranged from 55.7 mg/dL to 415.9 mg/dL (median: 132 mg/dL). Hyperglycemia in PICU was prevalent, with 125 (64.8%) patients having Gmax>110 mg/dL during their PICU stay and 35 (18.8%) having Gmax>200 mg/dL. Average PICU length of stay and total hospital length of stay grew as the maximum glucose levels rose among the four plasma glycemic ranges. The highest serum glucose range patient group also had the highest wound infection rates (14.3% and 11.4%). They concluded that hyperglycemia was prevalent among patients after major abdominal surgery in PICU and was correlated with increased PICU length of stay, total hospital length of stay.[7, 8]

Preissig CM et al surveyed 30 US pediatric ICUs from January to May 2009. Fourteen out of 30 centers believe all critically ill hyperglycemic adults should be treated, while 3/30 believe all critically ill children should be treated. Twenty-nine of 30 believe some subsets of adults with hyperglycemia should be treated, while 20/30 believe some subsets of children should receive glycemic control. A total of 70%, 73%, 80%, 27%, and 40% of centers believe hyperglycemia adversely affects outcomes in cardiac, trauma, traumatic brain injury, general medical, and general surgical pediatric patients, respectively. Sixty percent of centers believe hypoglycemia is more dangerous than hyperglycemia. Seventy percent listed fear of management-induced hypoglycemia as a barrier to glycemic control at their center. They concluded that considerable disparity exists between physician beliefs and actual practice habits regarding glycemic control among pediatric practitioners, with few centers reporting the use of any consistent standard approach to screening and management. Ulate KP et al determined whether a more permissive glycemic target would be associated with a decreased incidence of hypoglycemia but not increased mortality rates in critically ill pediatric patients. The peak and mean blood glucose measurements and duration of hyperglycemia were not different for survivors and non survivors in the first 24 hours after surgery. Non survivors had higher peak glucose levels and longer duration of hyperglycemia during the first 5 postoperative days, compared with survivors. Mortality rates were significantly higher for the moderate (38.8%) and severe (58.3%) hyperglycemia groups, compared with the euglycemia (6.02%) and permissive target (4.69%) groups. The incidence of hypoglycemia was significantly higher in the euglycemia group (31.8%), compared with the permissive target group (17.18%). They concluded that postoperative hyperglycemia is associated with increased morbidity and mortality rates in children after surgical repair of congenital heart defects. [9, 10]

CONCLUSION:

From the results of present study, we conclude that the risk of progression of stress hyperglycemia to diabetes mellitus is low; however, there is high prevalence of insulin resistance in these patients

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