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Original Research

Relationship between insulin metabolic disorders and pediatric stress hyperglycemia

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***ABSTRACT*:**

Background: Stress hyperglycemia (SH) commonly occurs during critical illness in children, even in those with previously normal glucose homeostasis. Based on the premise that SH during critical illness is possibly harmful, tight glucose control (TGC) to normalize blood glucose (BG) concentrations has emerged as a rational but unproven therapy to improve outcomes in critically ill children. **Aim of the study:** To study relationship between insulin metabolic disorders and pediatric stress hyperglycemia. **Materials and methods:** The present study was conducted in the Department of Pediatrics, MGM Medical College, Navi Mumbai, Maharashtra, India. For the study, we selected 70 patients admitted in the ward of Department of Pediatrics. Blood glucose greater than 200 mg/dl was considered as hyperglycemia. 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. **Results:** A total of 70 patients were included in the study. The mean age of the subjects was 9.32 years. The mean weight of the subjects was 25.65 kg, mean height is 1.16 m, mean BMI is 20.65 and mean systolic blood pressure is 110.87 mmHg. Glucose tolerance impairment was seen in 26 patients, BMI> 95^{th} percentile was seen in 19 patients, systolic blood pressure >95^{th} percentile was seen in 13 patients, HDL < 5^{th} percentile was seen in 14 patients, triglycerides >95^{th} percentile was seen in 11 patients, and insulin resistance was seen in 39 patients. **Conclusion**: According to results of this study, this can be concluded that the risk of progression of stress hyperglycemia to diabetes mellitus is high.

Keywords: Diabetes mellitus, stress hyperglycemia, insulin resistance

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INTRODUCTION:

Stress hyperglycemia (SH) commonly occurs during critical illness in children, even in those with previously normal glucose homeostasis. [1,2] Historically, SH during pediatric critical illness was considered to be, at best, an adaptive response that improved survival or, at worst, inconsequential.8,9 However, studies in children have challenged this assertion by observing that SH during critical illness is associated with poor outcomes. [3] Based on the premise that SH during critical illness is possibly harmful, tight glucose control (TGC) to normalize blood glucose (BG) concentrations has emerged as a rational but unproven therapy to improve outcomes in critically ill children. [4] Studies of TGC in critically ill adults have had mixed results, with some observing worse outcomes from TGC. Stress hyperglycemia typically resolves as the acute illness or surgical stress abates. [5] More recently, the use of glycated hemoglobin (HbA1c) has been recommended over oral glucose tolerance test as the preferred diagnostic testing in hospitalized patients with hyperglycemia. Measurement of an HbA1c during periods of hospitalization provides the opportunity to differentiate patients with stress hyperglycemia from

those with diabetes who were previously undiagnosed.[6] Hence, the present study was conducted to study relationship between insulin metabolic disorders and pediatric stress hyperglycemia.

MATERIALS AND METHODS:

The present study was conducted in the Department of Pediatrics, MGM Medical College, Navi Mumbai, Maharashtra, India. The study was approved from the institutional ethical board prior to commencement of the study. For the study, we selected 70 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:

A total of 70 patients were included in the study. **Table 1** shows the demographic data of the subjects. The mean age of the subjects was 9.32 years. The mean weight of the subjects was 25.65 kg, mean height is 1.16 m, mean BMI is 20.65 and mean systolic blood pressure is 110.87 mmHg. **Table 2** shows the metabolic profile of the patients. Glucose tolerance impairment was seen in 26 patients, BMI> 95th percentile was seen in 19 patients, systolic blood pressure >95th percentile was seen in 13 patients, HDL < 5th percentile was seen in 14 patients, triglycerides >95th percentile was seen in 11 patients, and insulin resistance was seen in 39 patients. The most prevalent component of metabolic syndrome in our study is insulin resistance. **[Fig 1]**

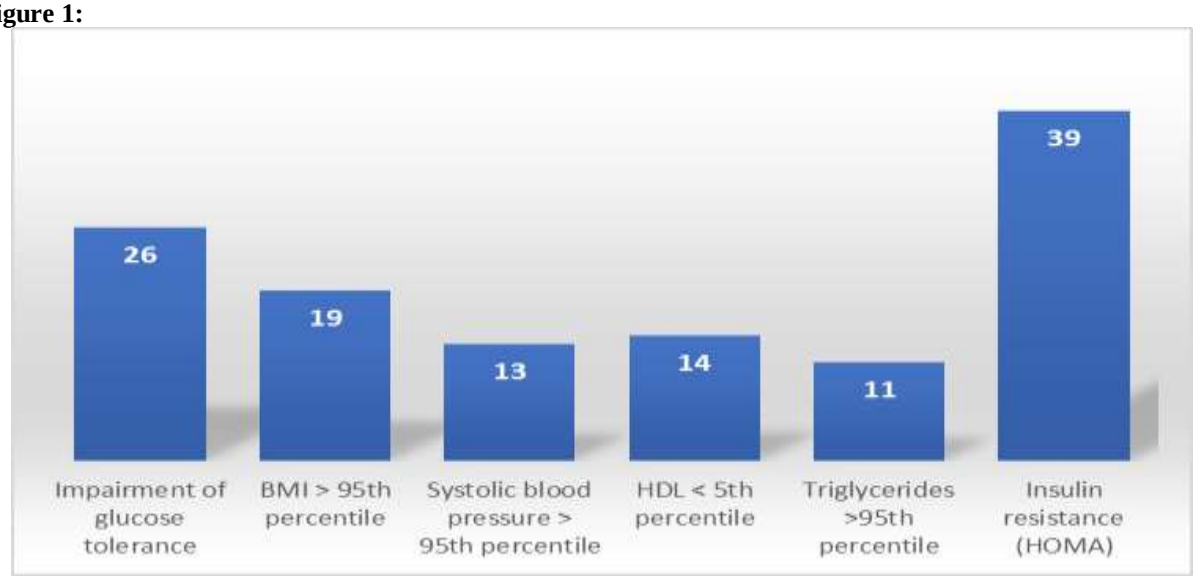
Table 1: Demographic data

Variables	Mean value
Age (years)	9.32
Weight (kg)	25.65
Height (m)	1.16
BMI	20.65
Systolic blood pressure (mmHg)	110.87

Table 2: Metabolic profile of the patients

Variables	Number of patients
Impairment of glucose tolerance	26
BMI > 95th percentile	19
Systolic blood pressure > 95th percentile	13
HDL < 5th percentile	14
Triglycerides >95th percentile	11
Insulin resistance (HOMA)	39

Figure 1:



DISCUSSION:

In the present study, we observed that glucose tolerance impairment was seen in 26 patients, BMI> 95th percentile was seen in 19 patients, systolic blood pressure >95th percentile was seen in 13 patients, HDL < 5th percentile was seen in 14 patients, triglycerides >95th percentile was seen in 11 patients, and insulin resistance was seen in 39 patients. The most prevalent component of metabolic syndrome in our study is insulin resistance. The results were compared to previous studies in the literature and were found to be consistent. Weiss SL et al determined the incidence and course of extreme stress hyperglycemia (ESH) in acute pediatric illness, including whether it is a marker of increased mortality or associated with subsequent development of diabetes mellitus (DM). They retrospectively reviewed a cohort of 55,120 consecutive visits over 6 years to a pediatric emergency department at which blood glucose concentrations were measured and report on visits with laboratory glucose 300 mg/dL (16.7 mmol/L) or greater without DM. There were 72 cases of ESH (incidence of 0.13%). Median age was 8.8 years; 63% were male. The most common diagnoses were respiratory illness (49%), trauma (15%), and seizure (8%), and 65% of patients had received glucose-influencing interventions before evaluation. Eighty-five percent were ill appearing, 60% were admitted to the intensive care unit, and half had acidemic pH values. The overall mortality rate was 22%. Despite treatment of hyperglycemia in only 8 patients, glucose concentrations decreased to 150 mg/dL (8.3 mmol/L) or less within 48 hours in 67% and before discharge or death in 85% of patients. Preceding symptoms and concurrent laboratory results were helpful to exclude diabetes, and none of the surviving patients with follow-up available went on to develop type 1 or 2 DM. in conclusion, although rare, ESH (≥300 mg/dL [16.7 mmol/L]) does occur in acute pediatric illness, in most cases is at least partially iatrogenic, and is a marker of severe illness and high mortality. Normoglycemia is typically restored quickly with treatment of the primary illness. No association was found with a subsequent diagnosis of DM. El-Sherbini SA et al studied the incidence of stress hyperglycemia in critically ill children and to investigate the etiological basis of the hyperglycemia based on homeostasis model assessment. This was a prospective cohort study in one of the pediatric intensive care units of Cairo University, including 60 critically ill children and 21 healthy controls. Serum blood glucose, insulin, and C-peptide levels were measured within 24 hours of admission. Homeostasis model assessment was used to assess β-cell function and insulin sensitivity. Hyperglycemia was estimated in 70% of patients. Blood glucose values ≥ 180mg/dL were associated with a poor outcome. Blood glucose levels were positively correlated with Pediatric Risk for Mortality (PRISM III) score and number of organ dysfunctions ($p = 0.019$ and $p = 0.022$, respectively), while insulin levels were negatively correlated with number of organ dysfunctions ($r = -0.33$, $p = 0.01$). Homeostasis model assessment revealed that 26 (43.3%) of the critically ill patients had low β-cell function, and 18 (30%) had low insulin sensitivity. Combined pathology was detected in 2 (3.3%) patients only. Low β-cell function was significantly associated with the presence of multi-organ dysfunction; respiratory, cardiovascular, and hematological dysfunctions; and the presence of sepsis. They concluded that β-Cell dysfunction appeared to be prevalent in our cohort and was associated with multi-organ dysfunction. [7, 8]

Sharma J et al studied and determined the prevalence and factors associated with stress hyperglycemia. A cross-sectional observational study was performed on 536 nondiabetic patients presented to the Intensive Care Unit (ICU) at Gandhi Medical College and allied Hamidia Hospital, Bhopal, between March 31, 2015, and May 28, 2015. A detailed history including demographic profile, presence of chronic disease, history of hospitalization and ICU admission, surgical status, and major reason for ICU admission (i.e., predominant diagnostic category) was collected. Hematological and other parameters based on profile of study population were also analyzed. Out of 536 patients, 109 (20.33%) had stress hyperglycemia. Out of 109 patients with stress hyperglycemia, 87 (16.23%) patients had glycated hemoglobin (HbA1c) <5.7% and 22 (4.10%) patients had HbA1c between 5.7% and 6.4%. Mean age of the study population was 40.27 ± 1.44 years, with male dominance. Mean random blood glucose level was 181.46 ± 3.80 mg/dl. Frequency of stress hyperglycemia was 24.13% in stroke, 19.54% in multiple organ dysfunction syndrome (MODS), 17.24% in chronic kidney disease (CKD), 12.64% in central nervous system (CNS) infection, 8.05% in chronic liver disease (CLD), and 8.05% in seizure patients. Association between stroke and stress hyperglycemia was significant. Association between hospital stay more than 7 days and stress hyperglycemia was significant in stroke patients, CKD patients, CLD, and MODS patients. They concluded that the factors associated with stress hyperglycemia were stroke, MODS, CKD, CNS infection, CLD, seizure patients, with prolonged hospital stay and expected proportion. De Cosmi V conducted review aimed to discuss the metabolic changes in critically-ill children and the potential of developing personalized nutritional interventions. Through a literature search strategy, we have investigated the importance of blood glucose levels, the nutritional aspects of the different phases of acute stress response, and the reliability of the available tools to assess the energy expenditure. The dynamics of

metabolism during stressful events reveal the difficult balance between risk of hypo- or hyperglycemia and under- or overfeeding. Within this context, individualized and accurate measurement of energy expenditure may help in defining the metabolic needs of patients. Given the variability of the metabolic response in critical conditions, randomized clinical studies in ill children are needed to evaluate the effect of individualized nutritional intervention on health outcomes. [9,10]

CONCLUSION:

According to results of this study, this can be concluded that the risk of progression of stress hyperglycemia to diabetes mellitus is high.

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