Stress Induced Hyperglycemia in a Term Baby Mimicking Diabetic Ketoacidosis with Stroke

Aliza Mittal, Ratan Gupta, Shobha Sharma, Kailash Chandra Aggarwal
Department of Pediatrics, VMMC and Safdarjung Hospital, New Delhi, India

ABSTRACT
Stress/sepsis induced transient hyperglycemia in the newborn may present with extremely high blood sugar values and may mimic neonatal diabetes mellitus. We present a case of neonatal septicemia with stress induced hyperglycemia mimicking neonatal diabetes mellitus. Extremely high blood sugar values up to 1529 mg/dL with metabolic acidosis were noted in a term good weight baby causing a diagnostic dilemma. It can be seen even in term babies, contrary to the belief that it occurs in preterm and small for gestation babies. Considering the prognostic implications it may cause it is important that hyperglycemia is promptly treated by insulin infusion.

Key words:
Hyperglycemia, insulin therapy, neonatal diabetes, stress

INTRODUCTION
Stress induced hyperglycemia is a known complication of Neonatal sepsis, but sometimes it may become very difficult to distinguish it from neonatal diabetes mellitus. We present a case of neonatal septicemia with stress induced hyperglycemia mimicking neonatal diabetes mellitus. Extremely high blood sugar values with metabolic acidosis were noted in a term good weight baby causing a diagnostic dilemma.

CASE REPORT
The present case report is about a 3 kg term neonate who presented on the 9th day of life with a history of fever for 2 days, lethargy and one episode of seizure. At admission, he was in a state of shock with severe dehydration. Anterior fontanel was bulging.

He was given two boluses of normal saline, radiant warmer care and intravenous antibiotics (cefotaxime and vancomycin) were started. Inotropic support with dopamine was given in view of septic shock. The blood sugar was 1529 mg/dL and arterial blood gases revealed mild metabolic acidosis (pH - 7.289 and HCO3 - 11.5). Urine ketones were however negative. Dehydration was corrected and thereafter considering the high blood sugar, the child was started on intravenous insulin infusion promptly at a dose of 0.1 IU/kg/h.

On evaluation, there was thrombocytopenia (platelet count -25,000) and serum procalcitonin was 3.10 ng/ml and C-reactive protein was 10, which was high and suggestive of septicemia. Lumbar puncture revealed a turbid cerebrospinal fluid (CSF), which was full of polymorphonuclear cells, CSF protein was 80 mg/dL and sugar was 67 mg/dL. Blood culture was positive for growth of *Staphylococcus aureus*. Urine culture, CSF culture and chest X-ray were normal. Hence, a diagnosis of late onset neonatal septicemia with shock with stress induced hyperglycemia was considered.

Considering neonatal diabetes as another possibility due to very high blood sugars, child was evaluated further and it was found that serum insulin and glucagon stimulated c peptide levels were respectively 4.00 mcU/ml and 2.57 ng/ml, which were normal. Glycosylated hemoglobin was 5%.

With supportive management, child improved as acidosis and hyperglycemia gradually resolved, there were no more seizures and urine output was adequate. Insulin infusion was slowly tapered as blood sugar normalized and it was stopped after 48 h. Child maintained normoglycemia hereafter and did not require insulin infusion any more.

Address for correspondence:
Dr. Ratan Gupta,
Department of Pediatrics, VMMC and Safdarjung Hospital,
New Delhi - 110 029, India.
E-mail: ratangupta100@yahoo.com

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Magnetic resonance imaging brain was done at 45 days of life which revealed cerebral venous thrombosis of the transverse sinus with hemorrhagic infarct in left temporal region [Figure 1]. The child has been under follow-up for 6 months now with normoglycemia and no neurological sequelae.

**DISCUSSION**

Hyperglycemia, defined as fasting blood glucose > 125 mg/dL is mostly seen in very low birth, small for gestation age infants and preterm babies receiving intravenous glucose infusion.[1] This is attributable to altered metabolism associated with immaturity, as well as the need for continuous parenteral nutrition. In these children, it may be triggered by respiratory distress, surgery, neonatal pain, sepsis and other stressful events. Hyperglycemia in preterm infants has been associated with increased rates of death, intraventricular hemorrhage (IVH), sepsis and retinopathy of prematurity and with increased lengths of hospital stay.[1] However, such a presentation in a term, good weight baby is uncommon.

The problem of hyperglycemia is manifested due to an increase in the osmolality (1 mosm/L rise is noted with every 18 mg/dL increase in blood sugar); particularly beyond 300 mosm/L. This is in the form of electrolyte disturbances, osmotic diuresis and in extreme form with IVH. The study by Louik et al. had discussed that the fluctuations in cerebral blood flow velocity markedly increase the risk of IVH and such fluctuations may be partially caused by rapid change in osmolality. Whether hyperglycemia causes IVH or vice versa is still controversial, but a plasma glucose level of more than 300 mg/dL is usually associated with a high risk of developing IVH.[3] However, there is a paucity of data in Indian population where more than 30% babies are low birth weight.

In a study carried out on 1171 newborns admitted to NICU by Chellani et al., the mean blood glucose level was 271.8 ± 75.33 mg/dL (range: 175-400 mg/dL) with a mean duration of hyperglycemia 60.6 ± 15.44 h (range: 48-96 h). In our case values as high as 1529 mg/dL were noted, which is uncommonly seen in term babies who are non-diabetic.

Stress factor responsible for causation of hyperglycemia includes sepsis due to *Escherichia coli* and Group B streptococci.[3] It can also be associated with hyperglycemia by catecholamine, cortisol influences on the mobilization of glycogen, gluconeogenesis and insulin response. On the other hand, endotoxins and cytokines may have a direct effect on insulin actions in septic infants.[4] Among drugs, methyl-xanthine which is most often used in preterm babies causes an increase in cAMP level resulting in activated liver glycogenosis.[3]

As per the cochrane database, it is possible that it is the sicker neonate, who is at higher risk for adverse clinical outcomes, who is more prone to hyperglycemia because of stress or metabolic injury to vital organs, especially the brain. It is also possible that it is hyperglycemia per se that is a cause of adverse clinical outcomes, especially if hyperglycemia is severe enough to cause significant plasma hyperosmolality resulting in fluid shifts from the intracellular to the extracellular fluid compartment. This is of particular concern with respect to the risk of cerebral bleeding. There is also some evidence of an adverse effect of severe hyperglycemia on neurologic outcome following cerebral ischemia in animals and adult humans as well as the neonate. Thus, in the very low birth weight/extremely low birth weight neonate with hyperglycemia, it is important to determine the benefits and risks of treating the hyperglycemia by either reducing the rate of glucose infusion or by administering exogenous insulin.

**CONCLUSION**

Based on the above report it can be concluded that stress due to sepsis induced transient hyperglycemia in the newborn may present with extremely high blood sugar values and may mimic neonatal diabetes mellitus. It can be seen even in term babies, contrary to the belief that it occurs in preterm and small for gestation babies. Considering the prognostic implications it may cause it is important that hyperglycemia is promptly treated by insulin infusion.

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