

Original article:

Prediction of neonatal hypoglycemia using cord blood C-peptide and cord HbA1c in infant Of diabetic mother

DR.Mitali Mahapatra* , DR.Rishav Raj**

Department of OBGY* and Pediatrics**

Name of the Institute/college: HI Tech Medical College , Bhubaneshwar , India

Corresponding author : DR.Mitali Mahapatra

Abstract:

Introduction: : Our aim was to find out the role of cord blood C-peptide and cord blood HbA1c in prediction of Neonatal Hypoglycemia in infant of diabetic mother.

Methodology: A Prospective Observational Study. All the mothers with diabetes mellitus and their newly born delivered in HI-TECH MEDICAL COLLEGE,BBSR in a period of 1 year from September 2013 to September 2014 were recruited for the study after prior consent . Newborn with following complication were excluded:1.Preterm 2. IUGR baby 3.Neonatal Sepsis 4. Birth Asphyxia 5. RDS 6. MAS 7. Babies with major congenital anomalies. 2ml of cord blood was collected in EDTA vial for Hba1c estimation and another 2ml of cord blood was collected in plain vial for estimation of cord blood c-peptide .As per protocol glucose monitoring was done in infant of diabetic mother to rule out hypoglycemia and fetal adverse outcome. As per American Academy of Pediatrics ,Neonatal Hypoglycemia is defined as follows : Less than 40 mg/dl (2.2mmol/l) during first 24 hrs of life. Less than 50mg/dl (2.8 mmol/l) after 24 hours of age.

Results: Umbilical Cord HbA1c is a good predictor of neonatal hypoglycemia. The Hypoglycemia in Infant of Diabetic mother was associated with raised cord blood c-peptide.

Keywords: Neonatal hypoglycemia, IDM, cord blood c-peptide, cord blood Hba1c.

Introduction:

In this modern era, obesity in childhood and in woman of child bearing age is one of the significant health burden . According to WHO, this health care problem is on the rise in both developed and developing nation .A sedentary life style, western diet and excessive food consumption are the principle cause of such phenomenon .

It is observed that perinatal morbidity and mortality has increased by leaps and bounds with pregnancies in obese and diabetic women . Diabetic mother has increased co-morbidities during pregnancy for instance neonatal hypoglycemia , respiratory distress

syndrome ,fetal macrosomia ,birth injuries and congenital anomalies in newborn and pre-eclampsia/hypertension to the mother .

In diabetic mother if there is poor glycemic control it will give rise to fetal hyperglycemia which in turn results in hyperplasia of islets of langerhans ,increased peripheral insulin receptors, a decreased glucagon response to hypoglycemia and delayed evocation of hepatic gluconeogenic pathway (1).

At delivery the transplacental supply of glucose is stopped and hypoglycemia in neonates occurs .Poor maternal glycemic control during the third trimester has been shown to be strongly and independently

correlated with neonatal hypoglycemia requiring intervention.

Glucose is an essential primary substrate for the substrate for the brain and its consumption by the brain cells is high . Because of this, neurons and glial cells are susceptible to hypoglycemia . The vulnerable areas are the parieto-occipital regions of the cerebral cortex. Less commonly involved are neurons of hippocampus , caudate nucleus and putamen .

Glial injury may give rise to subsequent disturbances in myelination (1). It has been seen that unrecognized postnatal hypoglycemia may lead to neonatal seizure. Fortunately, in most of these neonates ,hypoglycemia is transient and asymptomatic . However , if the diagnosis is missed and neonates fails to achieve normoglycemia ,it may become symptomatic and suffer long term complications of cerebral injury (3). So,it is useful to predict neonatal hypoglycemia from the state of neonatal hypoglycemic control.

Human c-peptide is a 31 amino acid chain and is secreted from beta cells of pancreas in equimolar ratio with insulin . Cord serum c-peptide levels are used as an index of fetal beta cell function rather than insulin levels , because degradation of insulin is increased in presences of slight hemolysis (5).Metzer BE et al (6) also found that frequency of neonatal hypoglycemia was higher with higher cord c-peptide levels and newborns with hypoglycemia tends to have higher frequency of cord c-peptide level of more than 90th percentile. In this way , c-peptide levels provide direct indication of endogenous fetal levels of insulin and could predict neonatal hypoglycemia in early neonatal life.

Patients and methods:

All the mothers with diabetes mellitus and their neonates delivered in HMCH, Bhubaneswar in a period of 1 year from September 2013 to September 2014 were recruited for the study after prior consent.

INCLUSION CRITERIA: A total 50 neonates born to diabetic mothers during sept 2013 to sept 2014 were studied.

EXCLUSION CRITERIA: Pre-term Babies, Babies with IUGR, Neonatal complications namely sepsis or birth asphyxia, MAS(Meconium aspiration syndrome), respiratory distress syndrome, Babies with congenital anomalies.

Neonates were screened for blood glucose at 4,6,8,12,18,24 hours of postnatal age . Out of 50 Neonates , 30 infants developed hypoglycemia at any time during the first 24 hrs of age . Another 20 infants did not developed hypoglycemia during the first 24 hrs.

Procedure for the collection of cord blood c-peptide and cord blood HbA1c . Cord was clamped from both the side after milking the umbilical cord . 2 ml of cord blood was collected from the placental side EDTA vial for estimation of cord HbA1c and another 2ml of cord blood was also collected in plain vial for estimation of c-peptide .

All these procedures were performed after informed consent from the parents and they were communicated that no additional blood samples would be collected ,no extra procedure would be done and no modification of the treatment plan would be made.

Results:

Of the 50 Patients , 30 developed neonatal hypoglycemia and rest 20 infants were normoglycemia

Table 1.1 Distribution of cases by number of infants with hypoglycemia

No. of cases	With hypoglycemia	% n=30
Male (30)	20	66.6%
Female (20)	10	33.3%
Total 50	30	100%

Table 1.2 Clinical characteristics of mothers and newborns

Characteristics of mothers	Cases
Age (\pm SD)	29.4 \pm 4.81
Wt(kg)(\pm SD)	61.17 \pm 10.17
Types of Diabetes	
GDM	12
Type 2 Diabetes	13
Type 1 Diabetes	5
Treatment of Diabetes	
Diet alone	5(16.6%)
Diet and insulin	25(83.3%)
Mode of delivery	
NVD	30
LSCS	20
Characteristics of newborn infants	
Birth weight in (kg)	3.5 \pm 7
Gestational age	37 \pm 1.26
Male	30
Female	20
Preterm	10
Term	40
AGA	10
LGA	40

Table 1.3 cord blood c-peptide in cases with hypoglycemia

Subject	With hypoglycemia	c-peptide	p-value
Cases	30	4.57±2.5	0.005

Table 1.4 laboratory data for HbA1c

Parameter	Without diabetes	Diabetes
HbA1c(mother)	4.2±1.9	>6.5±1.1
HbA1c (infant)	4.5±1.5	=6.4±1
Hypoglycemia	Nil	30

Discussion:

The present study aimed at the evaluation of the use of cord blood HbA1c and cord blood c-peptide as the marker for the prediction of neonatal hypoglycemia in infant of diabetic mother.

Interestingly , the present observed positive correlation between between cord blood HbA1c and c-peptide for predicting neonatal hypoglycemia and helped in quick assessment and further management . It is noted that 30 infants had high cord blood c-peptide and HbA1c and were subjected to hypoglycemia.

Neonatal hypoglycemia in association with hyperinsulinemia represents the crux of Pederson hypothesis and the concept has been validated repeatedly for offspring of mother with diabetes (7). In the present study the c-peptide the mean value noted was 4.57±2.50 in IDM who became hypoglycemia.

The HbA1c level was significantly high with mean >6.5 ±1.1 who were found to be diabetic and infants were subjected to hypoglycemia.

References:

1. McIntosh N, Helms P, Smyth R. Forfar and Areil’s Textbook of Paediatrics. 6th Edition ed: Churchill Livingstone; 2003.
2. Kline GA, Edwards A. Antepartum and intrapartum insulin management of type 1 and type 2 diabetic women: Impact on clinically significant neonatal hypoglycemia. Diabetes Res Clin Pract 2007; 77:223-30.

The significant correlation of increased cord blood insulin with neonatal hypoglycemia in IDM ,being observed by David G et al (8) and Knip et al (9). As c-peptide secreted in equimolar concentration with insulin , so this high insulin levels also represent the high c-peptide at the same time. Similar observation has also been reported by cooper et al 10.

The current study also revealed that HbA1c >6.5% helped in prediction of fetal macrosomia and neonatal hypoglycemia. Arumugam and Abdul Majeed 2011 who showed that HbA1c level>6.8% in late pregnancy has a good predictor of hypoglycemia in newborn.

Conclusion:

An increase in cord blood c-peptide is significantly associated with early postnatal hypoglycemia in babies born to diabetic mother . Cord HbA1c >6.5% significantly associated with neonatal hypoglycemia and fetal macrosomia (LGA>90TH PERCENTILE).

3. Sayeed MA, Mahtab H, Khanam PA, Begum R, Banu A, Azad Khan AK. Diabetes and Hypertension in pregnancy in a rural community of Bangladesh: a population based study. *DiabetMed*. 2005; 22(9): 1267-1271.
4. Lucas, A and Morley, R and Cole, TJ (1988) Adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia. *BMJ (Clinical Research Ed.)* 1988; 297 (6659): 1304 - 1308.
5. O'Rahilly S, Burnett MA, Smith RF, Darley JH, Turner RC. Haemolysis affects insulin but not C-peptide immunoassay. *Diabetologia*. 1987;30(6):394 –396.
6. Kuhl C, Andersen GE, Hertel J, Molsted- Pedersen L. Metabolic events in infants of diabetic mothers during the first 24 hours after birth. I. Changes in plasma glucose, insulin and glucagon. *Acta Paediatr Scand* 1982; 71: 19- 25.
7. Metzger BE. Hyperglycemia and adverse pregnancy outcome study: neonatal glycemia. *Pediatrics*. 2010 Dec; 126(6):e1545-52. Epub 2010 Nov 15.
8. Dawid g, Horodnicka-Jozwa A, Petriczko E, Biczysko-Mokosa A. Diabetes in pregnancy: cord blood insulin level and neonatal outcome in relation to maternal glycated haemoglobin A1c in last trimester of pregnancy. *Pediatr Endocrinol diabetes Metab* 2009;15(4):253-9
9. Knip M, Lautala P, Leppaluoto J, Akerblom HK, Kouvainen K. Relation of enteroinsular hormones at birth to macrosomia and neonatal hypoglycemia in infants of diabetic mothers. *J Pediatr* 1983; 103(4): 603-11.
10. Cooper M.J, Enderlein M.A, Tarnoff H, Roge C. L. Asymmetrical septal hypertrophy in infants of diabetic mothers. Fetal echocardiography and impact of maternal control. *Am J Dis Child* 1992; 146(2): 226-9.
11. Arumugam K, Abdul Majeed N. Glycated haemoglobin is a good predictor of neonatal hypoglycemia in pregnancies complicated by diabetes. *Malays J Pathol*. 2011;33(1):21