International Journal of Contemporary Pediatrics
Yashodha HT et al. Int J Contemp Pediatr. 2017 Mar;4(2):604-607
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20170717

Original Research Article

Influence of maternal HbA1C on fetal insulin levels

Yashoda H. T., Swetha B.*, Manasa G.

Department of Pediatrics, KIMS, Bangalore, Karnataka, India

Received: 12 January 2017
Accepted: 07 February 2017

***Correspondence:**
Dr. Swetha B.,
E-mail: swethareddy616@gmail.com

ABSTRACT

Background: Gestational diabetes is the most common medical complication during pregnancy. The objective of this study was to study the effect of maternal HbA1C levels on fetal insulin levels.
Methods: Study was conducted at KIMS. 57 babies born to eligible diabetic pregnant women aged between19 to 40 years with gestational age between 35 and 42 weeks were recruited. Multiple births, gestational age <34 weeks, steroids given within 24 hours before birth, delay of >20 minutes in cord blood collection, delay of >60 minutes before freezing of plasma were excluded. Maternal investigations (HbA1C) were collected from maternal records. Umbilical cord blood was collected immediately after delivery and insulin levels were measured.
Results: In this study, mean cord blood insulin levels were 7.83±3.53 µU/ml, mother's mean HbA1C levels were 6.47±1.26. Statistically significant association was found between maternal HbA1C levels and fetal insulin levels. (r 0.37; P 0.004).
Conclusions: Increased cord blood insulin levels were found in infants of diabetic mothers at birth, more so in large for gestation age babies, suggesting inutero fetal programming and hence strict control of maternal diabetes is recommended to decrease long-term fetal effects.

Keywords: GDM, HbA1C, Insulin

INTRODUCTION

Gestational diabetes is the most common medical complication during pregnancy.

Gestation diabetes is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy.

Prevalence of GDM range from 3.8% to 21% in different parts of the country and more in urban areas than rural areas.[1]

During in utero development fetus relies primarily on glucose as an energy substrate. There is a continuous supply of glucose even during maternal fasting because of 30% increase in hepatic glucose production in late gestation. Maternal insulin resistance during gestation results in lipolysis with increase in the availability of FFA to be used as adipogenic substrate in fetus. Therefore, understanding mechanisms through which a fetus growing in nutrient rich environment becomes insulin resistance is a major challenge. Based on the hypothesis of fetal programming, changes in maternal metabolism may affect distant metabolic dysfunction in offspring mediated through physiological and/or epigenetic mechanisms. In long term follow up studies, the offspring of women who are either obese or diabetic during pregnancy had higher incidence of obesity and type 2 diabetes. Assessment of insulin at birth may be particularly a useful way of assessing whether fetus was exposed to abnormally high levels of glucose in utero

there by resulting in increased insulin resistance and metabolic sequeale.

Glycosylated hemoglobin (HbA1c) is commonly used as a measure of long-term maternal blood glucose control. HbA1C is a stable Hb variant and reflects mean glycemia during the previous 3 months. It is a strong predictor of diabetic complications and cut off used is 6.5% to diagnose diabetes and can be used as point of care test.[2] A study performed by JOSLIN clinic showed a relation between elevated HbA1c in the first trimester and major anomalies in IDMs. Several studies have shown that early miscarriage is associated with poor glycemic control. HbA1c concentrations >7 %, was associated with a 3-fold increase in the spontaneous abortion rate.[3]

Assessment of insulin at birth may be particularly a useful way of assessing whether fetus was exposed to abnormally high levels of glucose in utero, resulting in increased insulin levels and metabolic sequelae. There is a need to identify increase insulin levels in babies as early as possible so that lifestyle measures such as healthy dietary habits and exercise could be introduced at the earliest in order to prevent the potential long term implications.

METHODS

In this prospective observational study conducted at KIMSH, during January 2015 to December 2015, after obtaining informed and written consent from the mothers, 57 eligible diabetic mothers aged between19 to 40 years with gestational age between 35 and 42 weeks and their babies were recruited. Mothers were subjected to detailed history and physical examination. Mothers records were reviewed for maternal age, height, pre-gestational weight, BMI, weight gain during pregnancy, gestational diabetic screening tests including HbA1C and diabetic control measures. Gestational age at birth was calculated from LMP, USG and Ballard scoring. Mothers with multiple births, gestational age <34 weeks, steroids given within 24hrs before birth, and delay of cord blood collection for >20min, delay of >60min before freezing of plasma were excluded. A total of 79 women with diabetes were eligible for the study of which 22 women were excluded, due to various reasons like one miscarriage, 3 twin pregnancies, 2 women with antenatal steroids being administered within 24 hours before birth, 7 women delivered before 34 weeks gestation,3 intrauterine death. 6 samples were not collected due to delay between sample collection and freezing. Finally, 57 women were eligible for the study.

Neonates' anthropometry was performed within 24 hours of birth. The weight was measured using a digital electronic weighing scale (to the nearest o.1kg) with minimal clothing. Small for gestational age (SGA) was defined as birth weight or birth crown heel length <10th percentile for gestational age or <2 standard deviations below the mean for infants gestational age, appropriate for gestational age (AGA) was defined as birth weight between 10th and 90th percentile for gestational age and large for gestational age (LGA) was defined as birth weight above two standard deviation for gestational age or above the 90th percentile.

Umbilical venous blood was drawn via syringe from the double-clamped cord immediately after delivery of the baby and before delivery of the placenta. Cord insulin concentration significantly decreased if the samples were taken in heparin containing tubes and stored at room temperature, but those samples taken in EDTA tubes and refrigerated remains stable for up to 48hrs. Sample haemolysis results in increased degradation of insulin. Various studies had shown significant (10%) degradation of insulin in samples which were either not collected from cord for more than 20 min or there was delay between sample collection and freezing for more than 60 min.[4-6]

Hence in this study cord blood was collected in EDTA tubes and centrifuged within 30 minutes and stored at (-80˚C) till assessment of insulin levels. Plasma insulin was measured by using a fully automated chemiluminescent immune assay (Roche, Germany). Hyperinsulinemia was defined as serum insulin levels ≥13.0 μU/ml.[7]

Statistical analysis

The cord blood insulin levels were correlated with maternal HbA1C using Pearson's correlation co-efficient. The results are considered statistically significant with P ≤0.05. Statistical software, SPSS V21.0 was used.

RESULTS

In the present study 57 mothers with GDM/Pre-gestational diabetes and their babies were included. Mean maternal age was 26.7±4.3 years, mean pre-pregnancy weight 62.0±9.73 kgs, mean HbA1C levels 6.47±1.26%. 11 (19.3%) GDM/type 2 diabetic mothers were overweight with BMI (between 23-24.9 kg/m^2) and 30 (52.6%) were obese with BMI (above 25 kg/m^2). Of infants born to diabetic mothers 10.5% were LGA, 10.5% were SGA and 79% were AGA. Mean HbA1C in diabetic mothers was 8.8%in LGA, 6.43% in AGA and 5.53% in SGA babies, showing moderate metabolic control of their diabetes. Studies had shown that large birth weight may reflect the influence of maternal diabetes in promoting both larger birth size and conferring offspring diabetic risk.[8] In this study mean cord blood insulin levels in infants were 7.83±3.53 μU/ml. Hyperinsulinemia was found in 9 (15.8%) infants. Out of 9 babies who had hyperinsulinemia, 6 (67%) were LGA, 1 (11.5%) were SGA and 1 (11.5%) were AGA. Statistically significant association was found between maternal HbA1C levels and cord blood insulin levels (r 0.37; P 0.004). In the present study there was moderately positive correlation between cord blood insulin levels of babies with HbA1C of diabetic mothers which were statistically highly

significant, showing the relation between cord blood insulin levels and maternal HbA1C.

Table 1: Mean values of variables.

	Mean	Std. deviation
Age of mothers (years)	26.65	4.37
Mother's weight in kg	62.02	9.73
Mother's height in cm	155.36	5.53
Maternal BMI (kg/m^2)	25.69	4.12
Weight gain during pregnancy	10.684	2.25
HbA1C	6.4682	1.3
Birth weight (kg)	3.24861	0.58
Cord blood insulin	7.83	3.5

DISCUSSION

Exposure to maternal diabetes in pregnancy is associated with high birthweight, increased childhood and adult obesity and increased risk of type 2 diabetes. In the present study there was positive correlation between maternal HbA1c levels and fetal cord blood insulin levels, which signifies the importance of maternal diabetic control in lowering cord blood insulin levels. Silverman et al reported a strong correlation between amniotic fluid insulin levels and increased BMI in adolescent aged 14-17 years indicating an association between islet cell activation in utero and development of childhood obesity which predisposes to obesity in adults.[9]

The results of the present study were comparable to other studies. Jenny A Westgate, Franzcog et al in New Zealand, in their study on newborns of 138 mothers with GDM, 39 mothers with Type 2 DM and 95 control mothers, found hyperinsulinemia in 29% of infants born to diabetic mothers and 31% of infants born to type 2 diabetic mothers compared to controls (3%) and also birth weight was higher in offspring of mothers with both GDM/Type 2 diabetes and cord blood insulin levels correlated with cord glucose and maternal HbA1C.[10]

Lindsay RS, Walker JD et al in their study on insulin like molecules in cord blood in relation to birth weight, maternal glycemia and cord glucose in 140 offspring of diabetic mothers and 49 0ffspring of control mothers, found that maternal diabetes was associated with increase in insulin levels in 63.5% compared to 50.3% in controls and insulin was more strongly related to birth weight, cord glucose concentration and maternal HbA1C.[11]

Weiss et al reported that a more pronounced and prolonged maternal hyperglycemia in IDM could be presumed to be the main reason for higher fetal and neonatal insulin levels in IDM.[12]

Beverly at al conducted a study on insulin, insulin resistance, insulin related peptides and found insulin concentrations to be significantly correlated with all measures like birth weight, length, head circumference and also found maternal glucose to be significantly associated with increased insulin concentration, reflecting that maternal glycemia was a major determinant of fetal insulin secretion.[13]

Limitations of the study were the sample size was smaller and further studies with larger sample size and long term follow up is required to establish the effect of insulin levels at birth with metabolic effects occurring in later childhood and adolescents.

CONCLUSION

In the present study, infants born to diabetic mothers had hyperinsulinemia and moderately positive correlation between maternal HbA1C and fetal insulin levels. Fetal insulin is potentially an important indicator of the metabolic effect of maternal diabetes on the fetus and later health of the child. So screening for glucose intolerance during pregnancy and appropriate intervention and consequently providing health care for all pregnant diabetic women are recommended in order to avoid or at least reduce the increased morbidity in their new-borns and children by developing simple, economical and effective prevention strategies.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Anjana RM, Pradeepa R, Deepa M. Prevalence of diabetes and pre-diabetes impaired fasting glucose and/or impaired glucose tolerance in urban and rural India: Phase I results of the Indian Council of Medical Research-India diabetes (ICMR-India) study. Diabetol. 2011;54:3022-7.
2. American Diabetes Association. Management of diabetes in pregnancy. Sec.12. In Standards of Medical Care in Diabetes-2016. Diabetes Care. 2016;39(Suppl. 1):S94-98.
3. Gary F. Cunningham, Leveno, Bloom. Williams Obstetrics ;24th Ed, Chapter 57; 2014:1125-1143.
4. Sapin R, Ongagna JC, Gasser F, Grucker D. Insulin measurements in haemolysed serum: influence of insulinase inhibitors. Clin Chim Acta. 1998;274:111-7.
5. Reimers TJ, McCann JP, Cowan RG, Concannon PW Effects of storage, hemolysis, and freezing and thawing on concentrations of thyroxine, cortisol, and insulin in blood samples. Proc Soc Exp Biol Med. 1982;170:509-16.
6. Brodal BP. The influence of haemolysis on the radioimmunoassay of insulin. Scand J Clin Lab Invest. 1971;28:287-90.

7. Simental-Mendía LE. Argelia, Birth-weight, insulin levels, and HOMA-IR in newborns at term, BMC Pediatrics. 2012;12:94.
8. Fall CHD, Stein CE, Kumaran K, Cox V, Osmond C, Barker DJP, et al. Size at birth, maternal weight, and type 2 diabetes in South India. Diabetic Med. 1998;15:220-7.
9. Catalano PM, Kirwan JP. Gestational diabetes and insulin resistance role in short and long term implications for mother and fetus. J Nutr. 2003;133:1674S-83S.
10. Jenny A. Westgate, Franzcog, Hyperinsulinemia in cord blood in mothers with type 2 diabetes and gestational diabetes mellitus in New Zealand. Diabetic Care. 2006;29(6):1345-50.
11. Lindsay RS, Walker JD. Insulin and insulin pro-peptides at birth in offspring of diabetic mothers. J Clin Endocrinol Metabol. 2002;88(4):1664-71.
12. Weiss, Hofmann. Fetal insulin balance; gestational diabetes and postpartal screening. Obstet Gynecol. 1984:64:65-68.
13. Shields BM, Bridget. Measurement of cord insulin and insulin-related peptides suggests that girls are more insulin resistant than boys at birth. Diabet Care. 2007;30(10):2661-66.

Cite this article as: Yashoda HT, Swetha B, Manasa G. Influence of maternal HbA1C on fetal insulin levels. Int J Contemp Pediatr 2017;4:604-7.