ORIGINAL RESEARCH PAPER
Volume-6 | Issue-9 | September-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

Maternal HbA1C as a marker in prediction of neonatal morbidities in gestational diabetics

Neonatology

Dr Aparna Balagopal	DCH, Senior Resident, Department of neonatology
PreethaRemesh	MRCPCH, Senior Consultant, Department of neonatology
Anand.M.R	MD, Senior Consultant, Department of Neonatology - Corresponding Author
Divia Nath Dip	NB, Consultant, Department of Neonatology
Dr Vishnu Mohan	MD, Consultant, Department of Neonatology

ABSTRACT

Gestational diabetes especially if poorly contolled is well known to cause neonatal morbidities.Neonatologist many often would not have an idea of how well contolled mothers diabetes was. In this prospective study we investigated the utility of intrapartum maternal HbA1C levels in the prediction of neonatal morbidities with special emphasis on neonatal hypoglycemia.Study which included 50 neonates showed association of elevated maternal HbA1C levels of more than 6.5 with neonatal morbidities of hypoglycemia,hypomagnesemia,hyperbilirubinemia and asymmetric septal hypertrophy.

KEYWORDS

Gestational diabetes, HbA1C, neonatal morbidities

Introduction

Gestational diabetes is well known to cause neonatal morbidities like macrosomia,birthinjuries,hypoglycemia,hypocalcemia,hypomagnesemia, polycythemia, hyperbilirubinemia, asymmetric septal hypertrophy and respiratory distress1. Suboptimal glycemic control has been noted to cause adverse neonatal outcomes2. The primary objective of our study was to find out the association of intrapartum maternal HbA1C levels and neonatal hypoglycemia. The secondary objectives were to study the association with other neonatal morbidities and to determine the ideal cut offs of maternal HbA1C values above which the risk of neonatal morbidities could be predicted.

Materials and methods

This prospective observational study was conducted in Aster Malabar Institute of Medical sciences,Kozhikode Kerala from May 2015 to April 2016.Sample size was calculated for the primary objective with the hypothesis that infants born to gestational diabetic mothers with HbA1C levels of more than 6.5% would have twice the risk of hypoglycemia than those born to mothers with HbA1C levels of less than 6.5%. This was based on a previous retrospective study where the rates of hypoglycemia were 58 % in those mothers with elevated 30 weeks HbA1C versus 28.6% in those with normal HbA1C3. A sample size of 50 was obtained to detect this difference with a power of 80% and two sided alpha of 0.05.Informed consent and ethical committee clearance were obtained for the study. Mothers with a diagnosis of gestational diabetes were included in the study. Mothers with other co morbidities like hypertension, heart diseases, pregestational diabetes were excluded. Blood samples were obtained after admission to labour room for anticipated labour. HbA1C levels were estimated by high performance liquid chromatographic method. After delivery,the newborn babies were admitted into the special care nursery. All babies had a detailed physical examination within 24 hours of life. Presence of respiratory distress or birth injuries were looked for. The birth weight of the babies was plotted against gestational age and babies were classified as large, small or appropriate for gestational age. Large for gestational age (LGA) was defined as birth weight greater than 90th percentile for gestational age, small for gestational age (SGA) as birth weight less than the 10th percentile for gestational age and macrosomia as birth weight more than 4000 grams. Babies born before 37 completed weeks of gestation were classified as preterm.Blood glucose levels of these infants were checked using a glucometer (Accucheck sensor, Roche, Germany) at [1, 3, 5, 9] and 12 hours after birth, and subsequently in babies who were hypoglycemic. If the glucometer value was less than 40 mg/dL, plasma glucose estimation was performed for confirmation. Hypoglycemia was defined as a blood glucose level of less than 40 mg/dL in any infant regardless gestational age and whether or not symptoms were present. Blood samples for measuring PCV, hemoglobin , serum ionized calcium, serum magnesium, serum bilirubin levels were taken during NICU stay. Polycythemia was defined as the presence of a venous hematocrit more than 65% or a venous hemoglobin concentration in excess of 22.0 g/dL. Hypocalcemia was defined as total serum calcium level less than 7 mg/dL(<1 mmol/L) in preterms and <8 mg/dL (<1.2mmol/L) in term babies. Hyperbilirubinemia was defined as a serum bilirubin level requiring phototherapy as per American Academy of Pediatrics charts. Echocardiogram was done for all babies. Relevant demographic, maternal and neonatal details were filled into a standard proforma and entered into Microsoft excel. Statistical analysis was done using the SPSS software version 17. Differences between qualitative variables were tested with the chi-square test and Fischer exact test. t-test and Mann-Whitney U test were used for continuous variables. p value of <0.05 was considered as statistically significant.ROC curve was plotted for those variables showing statistical significance on primary analysis.

Results

The study population consisted of 23 (46%) term and 27 (54%) preterms. 31 (62%) were male and 19 (38%),female. 41(82%) of the deliveries were caesarean sections and 9 (18%) vaginal deliveries. Most (40) of the babies were AGA's, 2 were SGA's 8 LGA's. 4 babies had macrosomia. One baby developed birth injury in the form of erb's palsy. None of the babies had birth asphyxia. 18(36%) mothers had HbA1c levels more than 6.5% whereas 32 (64%) had HbA1c levels less than or equal to 6.5%.Hypoglycemia, hypomagnesemia, hyperbilirubinemia, polycythemia and asymmetric septal hypertrophy were found to be more in babies born to mothers with elevated mothers with elevated HbA1C (table1). Cut off levels of maternal HbA1C obtained by plotting ROC curves are shown in table 2 .

Discussion

Results of our study show that maternal HbA1C levels obtained upon admission to labour room might help in predicting certain neonatal morbidities. HbA1C levels indicate the glycemic control during the preceding 3 months. Pregnancy has been known to be associated with lower HbA1C levels in several studies4.This is often due to higher physiological turnover of erythrocytes5. Most guidelines indicate adequate metabolic control in gestational diabetics by a HbA1C value of < 7%. NICE guidelines suggesta cut off of 6.1% 6. In this study we chose a cut off of 6.5% ie midway between both. Few other studies have reported the utility of HbA1C to predict neonatal morbidities. Obese mothers without GDM with HbA1C > 5.7% were reported to have more LGA babies7. In a study of 150 mothers

with gestational and pregestational diabetes a late pregnancy HbA1C value of >6.8% was found to be an ideal threshold to predict neonatal hypoglycemia[8].

Other studies report increase in neonatal morbidities with HbA1C values of > 8%9 and > 7% 10 respectively. It is of importance to note that most of the babies in our study sample were AGA's which indicate that even such babies are predisposed to morbidities. ROC curve analysis yielded good area under the curve only for the variables of hypomagnesemia, polycythemia and asymmetric septal hypertrophy. However we reiterate that as the sample size was calculated for the primary objective alone, further studies with larger sample sizes may yield better results Obtaining maternal HbA1C in gestational diabetics from the labour room will help the neonatologist to predict neonatal morbidities even when the antenatal follow ups were done elsewhere.

Table I . Maternal HbA1C Levels and Neonatal Morbidities

Variable	HbA1C > 6.5% n = 18	HbA1C <6.5% n = 32	p value
Hypoglycemia	6 (33)	2 (6.3)	< 0.05
Hypomagnesemia	5 (28)	1(3.1)	< 0.05
Hyperbilirubinemia	10 (55)	6 (19)	< 0.05
Polycythemia	5 (27)	0	< 0.05
ASH #	7 (38)	2 (6.3)	< 0.05
Hypocalcemia	6 (33)	6 (19)	> 0.05
RDS	5 (28)	12 (37)	> 0.05
Birth injury	1 (5.6)	0	> 0.05
Macrosomia	4 (22)	0	> 0.05

* Numbers in brackets indicate percentage
# Asymmetric septal hypertrophy

Table II. HbA1C Ideal Cut Offs

Variable	HbA1C levels	AUC	Inference
Hypoglycemia	6.8	0.805	Good
Polycythemia	6.6	0.858	Good
ASH	6.18	0.839	Good
Hypoglycemia	6.8	0.75	Fair
Hyperbilirubinemia	6.8	0.778	Fair

AUC = area under the ROC curve

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