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A clinical study of neonates of diabetic mother with special reference to blood glucose levels

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Abstract
Background: Diabetes is the most common medical complication during pregnancy, yet guidelines regarding the care of these infants of diabetic mother are not well established.
Objectives: To assess the spectrum of immediate complications of IDMs especially hypoglycemia, to find out the association between glucose levels in the mother at different periods of gestation, cord blood glucose and blood glucose levels in the neonate.
Methods: A prospective cohort study was done in Krishna Institute of Medical Sciences, Karad involving 75 consecutive live born infants of diabetic mothers. Maternal data was obtained from antenatal records. The infant was subjected to glucose estimation at predetermined intervals, screened for other morbidity patterns and followed up at early infancy.
Results: The commonest complications were congenital anomalies (most of which were minor) and hyperbilirubinemia both occurring in 42%. Hypoglycemia was found in 24%, usually asymptomatic, occurred within first 2hrs of life and responded to enteral feeds. Neonatal glucose levels moderately correlated with cord blood glucose ($r=0.543$; $p<0.001$) but not with intrapartum or antenatal glucose values.
Interpretation and conclusion: Infants of diabetic mother are high risk neonates requiring intensive monitoring but their blood glucose measurements may be limited to initial 2 hrs. minimising trauma and expense. Routine measurement of cord blood glucose and optimal glycemic control in the mother may be indicated to predict and prevent hypoglycemia. The short term prognosis appears to be bright in these infants.

Keywords: substituted Li ferrite, magnetostatic and spin waves, microstrip array antenna, X-band frequency range

Introduction

Diabetes is the most common medical complication in pregnancy. It affects about 1 to 5% of all pregnancies. It may antedate pregnancy (progestational diabetes) or may be detected for the first time during pregnancy (gestational diabetes). The prevalence of diabetes is increasing globally and India is no exception. Diabetes mellitus (DM) is a chronic metabolic disorder due to either insulin deficiency (relative or absolute) or due to peripheral tissue resistance to the action of insulin. World Health Organization (WHO) has predicted that between 1995 and 2025, there will be a 35% increase in the world wide prevalence of diabetes.

The IDMs are at an increased risk for peri-conceptional, fetal, neonatal and long term morbidities. Short-term neonatal complications, such as hypoglycemia, RDS, hypocalcemia, hypomagnesemia, hyperbilirubinemia, are related mainly to fetal hyperinsulinemia, hypoxemia, and prematurity. Long-range complications include an increased rate of childhood and adolescent obesity, impaired glucose tolerance or diabetes mellitus, and subtle neuropsychological dysfunctions.

The causes of the fetal and neonatal sequelae of maternal diabetes are likely multifactorial; however, many of the perinatal complications can be traced to the effect of maternal glycemic control on the fetus and can be prevented or at least reduced through meticulous prenatal and intrapartum care.

In India, where most pregnant women are brought to hospitals for the first time in labour, there is an important need to know if the immediate neonatal complications especially hypoglycemia in IDMs could be predicted by simple bed-side tests like intrapartum or cord blood glucose levels. This knowledge will not only help in categorisation of these at-risk newborns but also may help in further management in a resource limited setting.

The present study was conducted in infants born to diabetic mothers at KIMSDU, Karad from July 2016 to October 2017. It focuses on the immediate neonatal and short range complications of these infants with special reference to hypoglycemia and the extent to which it is related to maternal glycemic control, intrapartum and cord blood glucose levels.

Methodology

All consecutive live born infants born to diabetic mothers in Krishna Institute of Medical Sciences, Karad during the study period (July, 2016 to October 2017) formed the study population. The study was approved by the hospital ethical committee. Data regarding the diabetic status of the mother was obtained from antenatal records. Diabetic mothers were grouped into two categories: pregestational (diagnosed before pregnancy) and gestational DM.

Gestational diabetes was diagnosed based on Carpenter and Couston Criteria after an oral glucose tolerance test, i.e.; Fasting- 95mg/dl, 1 hour-180mg/dl, 2 hours-155mg/dl, 3 hours-140mg/dl. If two or more values were met or exceeded, the diagnosis of GDM was established.

Inclusion criteria

All consecutive infants born to mothers with Gestational Diabetes and Pregestational (Type 1 and Type 2) diabetes in KIMS during the study period.

Exclusion Criteria

- Infants where detailed maternal history is unavailable.
- Stillborn babies of diabetic mothers.

The glycemic status of the pregestational diabetic mothers was ascertained based on the serial estimation of fasting glucose levels. Each patient's fasting blood glucose values were averaged, yielding one mean value per patient. Blood glucose control was defined according to American College of Obstetricians and Gynaecologists guidelines: a mean fasting value of < 95 mg/dl. Two groups were identified: women with blood glucose averages within the recommended guidelines (optimal control) and women with blood glucose averages higher than the recommended guidelines (suboptimal control). Informed consent was obtained from all the mothers. Mothers' antenatal history and other associated obstetrical and medical problems were noted.

All the deliveries were attended by paediatrician and the babies evaluated first hand to avoid observer bias. The baby was shifted to the NICU and its blood glucose levels monitored at regular intervals (0, 1,2,3,6,12,24,36 and 48hrs) for first 48 hours of life by the standard heal prick using glucometric reagent strip method with the same glucometer for uniformity.

At admission, weight was recorded using digital weighing scale (to nearest 10gms). The babies grouped as SGA, AGA or LGA depending on the birth weight and gestational age according to growth charts. Data regarding detailed examination of the new born was collected in a predesigned proforma. Congenital anomalies were identified clinically and supported by 2D-Echocardiography. Respiratory distress was defined as respiratory rate of >60/min and/ or presence of subcostal and intercostal retractions. Hypoglycemia was defined as a blood glucose level less than or equal 40 mg/dl in any infant, regardless of gestational age and whether symptomatic or not.

IV dextrose was administered only if the baby was symptomatic or unable to take orally or if blood glucose levels were <20mg/dl. Venous hematocrit and serum calcium levels were measured if clinically relevant, in the laboratory by automated analyser. Polycythemia was diagnosed if venous hematocrit was greater than 65%. Hypocalcemia was defined as serum calcium level less than 7mg/dl. S.Bilirubin estimation was done in the biochemical laboratory if the neonate had clinical jaundice and repeated if necessary.

Chest x-ray and arterial blood gas analysis was done if baby had significant respiratory distress and 2D-echocardiography was done if cardiac disease was suspected by the pediatrician. Other investigations like Serum electrolytes, indirect ophthalmoscopy for ROP, neurosonogram, sepsis screen, and USG Abdomen were done if relevant. The baby was treated as per standard NICU guidelines of the hospital and shifted to mothers' side when stable.

Statistical Methods

Descriptive statistical analysis has been carried out in the present study. Significance is assessed at 5% level of significance. Student "t" test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups-Inter group analysis on metric parameters. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups and Microsoft Word and Excel have been used to generate graphs, tables etc.

Results

Out of a total of 2012 deliveries during the study period at Krishna Institute of Medical Sciences, Karad a total of 83 mothers with either progestational or gestational diabetes mellitus delivered 83 live born singleton neonates. Out of which 8 were excluded because of lack of proper data and remaining 75 were analysed.

Table 1: Gender distribution of study subjects

Gender	No. of Newborns (75)	%
Male	49	65
Female	26	35

Table 2: Mode of delivery of neonates

Mode of delivery	Newborns (n=75)	%
Normal	18	24
LSCS (Elective)	43	57
LSCS (Emergency)	14	19

Table 3: Classification according to birth weight and gestational age

Birth Weight	Number of newborns	%
SGA	3	4.0
AGA	61	81
LGA	11	15

Table 4: Comparison of Mean glucose levels- Intrapartum blood glucose of mother, Cord blood glucose and blood glucose of neonates

Blood Glucose at:	All Subjects	Pregestational	Gestational	P value
0 hour	60.02±18.46	58.65±16.82	59.99±19.28	0.626
1 hours	66.31±25.84	54.46±24.01	71.16±25.18	0.030*
2 hours	77.82±36.68	65.26±22.73	83.42±40.28	0.108
3 hours	87.16±47.57	80.81±33.9	89.75±52.67	0.547
6 hours	89.83±39.89	84.57±21.76	92.43±45.61	0.544
12 hours	85.98±21.68	91.38±28.04	83.67±18.34	0.254
24 hours	89.46±24.94	81.47±24.68	92.85±24.61	0.135
36 hours	88.76±24.57	79.37±18.34	93.25±25.97	0.073
48 hours	85.44±17.94	84.87±20.79	85.28±16.92	0.924

- Two-thirds of the infants in the study were between 2.5-3.5 kg.
- More than 3/4th of neonates were born at term (76%).
- It was observed that 70% of the mothers in the study had GDM and in the rest DM was diagnosed prior to pregnancy.
- The maternal age ranged from a minimum of 20 yrs. to a maximum of 40 yrs. with majority being in the age group of 20 to 34 yrs.

- More than half of the mothers had comorbid medical/obstetric conditions. The most common being PIH (18%). 8 mothers had vaginal candidiasis and 6 had anemia requiring treatment.
- At birth, the percentage of babies having externally identifiable congenital anomalies and audible murmur was 20% each, whereas 18% of babies had respiratory distress.
- The commonest external congenital anomaly was hairy pinna which was seen in 11 neonates.
- The commonest cardiac anomaly taken individually was ASD seen in 21 infants, next was PDA found in 15 babies followed by VSD which was seen in 2 child. 3 babies had associated PHTN diagnosed on echo.
- There was no significant difference in birth weights between those infants who developed hypoglycemia and those who remained normoglycemic.
- Majority of the babies (78%) were discharged from NICU within 4 days of admission and only 6% required prolonged stay for >1week.
- The comparative analysis of intrapartum glucose, cord blood glucose and blood glucose of neonates showed no significant difference in the 2 groups except for blood glucose at 1hr, which was significantly low in progestational IDM's.

Table 5: Complications of IDM

Complication	All Subjects	Type of DM		P value
		Pregestational (n=23)	Gestational (n=52)	
Macrosomia	11(14%)	3 (13.3%)	8 (14.3%)	1.000
Hypoglycemia	18 (24%)	9 (40%)	9 (17%)	0.136
CHD	24 (32%)	8 (34.7%)	16 (30.7%)	0.751
Sepsis	21 (28%)	7 (33.3%)	14 (25.7%)	0.733
RDS	2 (2%)	2 (8.6%)	0	0.654
Hypocalcaemia	3 (6%)	1 (6.7%)	2 (5.7%)	1.000
Hyperbilirubinemia requiring phototherapy	29 (38.7%)	10 (43.4%)	19(36.5%)	0.749

- Though the incidence of hypoglycemia, cardiac anomalies, sepsis, Hyperbilubinemia was more in the pregestational group, none of the differences were statistically significant.
- Hypoglycemia was seen only till 2 hrs. after birth in pregestational IDMs and till 1hr of life in gestational IDMs. There was no significant statistical difference in the incidence of hypoglycemia between the two groups, though a higher proportion of pregestational IDMs became hypoglycemic.
- There was no significant difference between the number of SGA, AGA or LGA babies between pregestational and gestational diabetics, although both the SGA babies belonged to the pregestational group.
- The overall mean duration of diabetes in pregestational group was 24 months, and in gestational group was 3 months. The mean duration of maternal diabetes was similar in infants who developed hypoglycemia and those who did not.
- The follow up rate was 90% and nearly 3/4th of the infants were normal. The major findings on follow up examinations were persistence of CHD's. The preterm child with RDS had developed ROP on follow up.

Discussion

The effective control of diabetes mellitus with insulin has led to an increasing number of diabetic women entering the reproductive age. On the other hand, the prevalence of new-onset diabetes is increasing in younger population. The infants of these mothers are predisposed to increased morbidity and mortality. In developed countries, there has been a significant improvement in the outcome of diabetic pregnancy due to improvement in the antepartum surveillance, better metabolic control and improved neonatal care. The management of newborns born to diabetic mothers still poses a major challenge in our country. Comprehensive care of pregnant women with diabetes mellitus has been extensively described, yet guidelines regarding the care of the infant are less well established. Hypoglycemia is the commonest and most dangerous of all metabolic abnormalities in IDMs. This prospective study was undertaken to analyze the neonatal complications of IDMs especially hypoglycemia and its probable correlations.

Conclusion

Our prospective cohort study has shown that in spite of intensive management of maternal diabetes, the infants of diabetic mother continue to be a high-risk population. Hence, they are best delivered and managed at a tertiary care centre capable of providing intensive monitoring and therapy. The major congenital anomalies were cardiac, occurring in as high as 32% of the subjects. Hyperbilirubinemia requiring phototherapy is an often overlooked complication of IDMs seen in 39%. Hypoglycemia continues to be a significant cause of morbidity in these babies. It tends to be asymptomatic or with subtle signs and seen only in early postnatal life within 2 hrs. Most often it could be managed by enteral feeds but remains difficult to predict on the basis of birth weight, duration of maternal diabetes or her antenatal glucose levels. Repeated estimations of blood glucose may be unnecessary after 2 hrs. as recurrent or late episodes of hypoglycemia are unlikely. Cord blood glucose level measured immediately at birth correlates with early postnatal glucose measurements and may be a predictor for hypoglycemic episodes when low. Therefore, optimal care of infants of diabetic mothers is based on prevention, early recognition, and/or treatment of neonatal morbidities.

Adequate glycemic control before and during pregnancy is crucial to improve the outcome of neonates born to diabetic mothers. Improving glycemic control of women during the

periconceptional period and strict control of diabetes throughout pregnancy with regular follow up with obstetricians and physicians remains the only way of improving the maternal and neonatal outcome.

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