Correlation of glycemic control in newborn at birth to maternal glycemic control

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Received - 23 December 2019 Initial Review - 17 January 2020 Accepted - 28 February 2020

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a common endocrine disorder of pregnancy with an incidence of approximately 1 in 1000. Perinatal outcomes and long-term sequelae in infants of diabetic mothers (IDM) are related to onset and duration of glucose intolerance and severity of disease in mother. O**bjective:** The objective of the study was to study the correlation of glycemic control in newborn to maternal glycemic control (glycosylated hemoglobin [HbA1c] levels). The occurrence of congenital malformations and other neonatal complications was also studied. **Materials and Methods:** A longitudinal study was carried out at a tertiary hospital of Central India from November 2018 to October 2019 and a total of 47 cases which were admitted during the study period were included in the study. All babies born either gestational or type 1 or type 2 diabetic mothers were included in the study. The sample size was calculated to be 38. Statistical analysis was done using Epi Info 7.1. Poor maternal glycemic control during the 3rd trimester has been shown to be strongly and independently correlate with neonatal hypoglycemia. Neonatal HbA1c correlates well with maternal HbA1c level after birth. **Results:** Poor maternal glycemic control during the 3rd trimester has been shown to be strongly and independently correlate with neonatal hypoglycemia. Neonatal HbA1c correlates well with maternal HbA1c level after birth. There was no statistically significant difference found between mean birth weight and gender ($p>0.05$) in IDM. **Conclusion:** It was concluded that IDM babies are at risk of hypoglycemia if the mother's HbA1c level goes beyond 6.5%. There was no significant correlation between the duration of diabetes and hypoglycemia and other congenital anomalies associated with maternal diabetes.

Key words: *Fetal anomalies, Gestational diabetes mellitus, Glucose intolerance, Glycemic control, Glycosylated hemoglobin, Hypoglycemia, Macrosomia*

Diabetes mellitus (DM) is defined as a syndrome characterized by disorder in metabolism of carbohydrates, proteins, and lipids, which results from absolute or relative lack or decreased efficacy of insulin in the body. The incidence of diabetes in pregnancy is approximately 1 in 1000 of the overall number of pregnancies [1]. Hyperglycemia in the fetus results in the stimulation of insulin, insulin-like growth factors, growth hormone, and other growth factors, which, in turn, stimulate fetal growth and deposition of fat and glycogen [2]. Perinatal outcomes and long-term neurologic sequelae in infants of diabetic mothers (IDM) are related to the onset and duration of glucose intolerance. Maternal glycosylated hemoglobin (HbA1c) levels have been found to be directly correlated with the occurrence of congenital malformations and other neonatal complications [3].

Among the various metabolic consequences observed in IDM, hypoglycemia is the most common and most serious because of its association with both acute decompensation and long-term neuronal loss. Most IDMs are prone to develop severe but asymptomatic hypoglycemia during the first postnatal hours [3]. Poor glycemic control in the diabetic mother results in fetal hyperglycemia which ultimately results in hyperplasia of the islets of Langerhans, increased peripheral insulin receptors, a decreased glucagon response to hypoglycemia, and a delayed evocation of hepatic gluconeogenic pathway [4]. At delivery, the transplacental supply of glucose is stopped and as a result, hypoglycemia in the neonate occurs.

Poor maternal glycemic control during the 3rd trimester has been shown to be strongly and independently correlated with neonatal hypoglycemia requiring intervention [5]. However, in most of these neonates, hypoglycemia is transient and asymptomatic. However, timely diagnosis is important as the neonate might fail to achieve normoglycemia, may become symptomatic and suffer long-term complications of cerebral injury. Thus, the determination of fetal hypoglycemia from the state of maternal glycemic control is important [6]. The present study was conducted to study the correlation of glycemic control in newborn at birth in relation to maternal glycemic control. The occurrence of congenital malformations and other neonatal complications was also studied.

MATERIALS AND METHODS

A longitudinal study was carried out at a tertiary hospital of Central India from November 2018 to October 2019. The study population

consisted of IDM either gestational (gestational DM [GDM]) or type 1 (T1DM) or type 2 (T2DM) DM in our tertiary care hospital. Prior Institutional Ethics Committee clearance was obtained and written consent was obtained from the parents or legal guardians before recruitment in the study. Mothers, whose HbA1c was not tested or who did not give consent, were excluded from the study. Sample size was calculated by the formula: $N = \{(Z\alpha + Z\beta)/C\}\ 2 + 3 = 38$ according to the study by Gouédard *et al*. [7].

A complete history was taken to know the duration and type of DM in the mother. Detailed anthropometry of the infants was taken and they were classified as appropriate, small, or large for gestational age (AGA, SGA, and LGA) as per Lubchenco's chart. Maternal HbA1c was done before delivery by high-performance liquid chromatography (HPLC). HbA1c of the newborn was done at 24 h after birth by HPLC. Random blood sugar was determined as per protocol for IDM at 0, 1, 2, 3, 6, 12, 24, and 48 h of life by glucometer. 2D ECHO was performed for all infants to detect any structural or functional abnormality of the heart. Statistical analysis was done using Epi Info 7.1. $p<0.05$ was considered statistically significant.

RESULTS

We considered a total of 47 cases which were admitted in our setup during the study period. Demographic profile of the study population is presented in Table 1. There was no significant difference found between mean birth weight and gender ($p>0.05$) in IDM.

There were 72.3% of AGA infants, 23.4% were SGA, and 4.3% were LGA. Mean HbA1c% of neonates was 5.89% with standard deviation (SD) of 0.64 and mean maternal HbA1c was 5.6% with SD 0.681. This difference was not found to be statistically significant ($p>0.05$) which infers that maternal glycemic control is well transmitted to newborns.The periodic monitoring of HbA1c levels provide a useful way of documenting the degree of control of glucose metabolism in diabetic patients [8].

Table 2 shows that there is significant correlation between maternal and neonatal MEAN HbA1c levels.

The mean blood sugar 0 h was 78.72 mg/dl and at 48 h was 74.98 mg/dl. As shown in Table 3, repeated measure ANOVA showed statistically non-significant difference in blood glucose levels at various timings after birth ($p>0.05$) which means that blood sugar in neonates was not different from birth to 48 h.

Table 4 shows that there was a significant correlation found at maternal HbA1c level of more than 6.5. This implicates that as maternal HbA1c increases, neonatal blood sugar level decreases beyond 6.5%, which shows that uncontrolled GDM puts the baby at a risk of hypoglycemia. Neonatal HbA1c did not correlate with blood sugar level at 48 h. There was no case of congenital anomalies in our study population.

DISCUSSION

This study was taken to study the significance of cord blood HbA1c in predicting postnatal hypoglycemia. Fetal hyperglycemia plays a major role in the development of postnatal hypoglycemia as well as macrosomia and other congenital malformation. In the present study, most of the mothers had controlled GDM, and hence, we did not find any case of hypoglycemia, congenital anomalies, and significant macrosomia which are the main morbidities related to uncontrolled GDM.

Koedak *et al*. assessed glycemia by the measurement of HbA1c and found it to be a valid index of glycemia which was in accordance with the present study, as all mothers who had HbA1c <7% had a good control. In the present study, there was male predominance with 66% of males. This was in accordance with the study by Haider *et al*. where there were 58% of males [9]. They also documented hypoglycemia in 28% of cases and association of asymmetrical septal hypertrophy along with macrosomia which

Table 1: Distribution of mean birth weight and gender in IDM

Gender	Number	Birth weight (Mean±SD)	Std. error of mean	*t*-value	*P*-value
Male	31 (66)	2.733±0.393 kg	0.0706	0.595	0.555
Female	16 (34)	2.637±0.715 kg	0.1787		
Total	47 (100)	2.699±0.519 kg	0.0757		

IDM: Infants of diabetic mothers, SD: Standard deviation

Table 2: Correlation between maternal and neonatal mean HbA1c

HbA1c levels	Number	Mean	SD	Correlation	*P*-value
Neonate HbA1c (%)	47	5.89	0.64	−0.201	0.180
Maternal HbA1c (%)	47	5.60	0.68		

HbA1c: Glycosylated hemoglobin, SD: Standard deviation

Table 3: Mean neonatal blood glucose levels at different timings after birth

Time period	Neonatal blood glucose levels	
	Mean	SD
0 h	78.72	16.069
1 h	76.04	9.558
2 h	75.66	9.111
3 h	74.72	8.907
6 h	75.57	11.284
12 h	75.49	9.771
24 h	74.02	7.674
48 h	74.98	9.361

SD: Standard deviation

Table 4: Correlation of maternal HbA1c with neonatal blood sugar levels

Maternal HbA1c (%)	Blood sugar (mg/dl) at 48 h			
	Number	Mean±SD	*P*-value	Correlation
<5.5	18	75.22±10.82	0.64	0.0715
5.5–6	15	74.47±9.75		−0.051
6–6.5	11	76.91±7.27		−0.155
>6.5	3	69.00±3.61		−0.355
Total	47	74.98±9.36		−0.039

SD: Standard deviation, HbA1c: Glycosylated hemoglobin

was not witnessed in our study, as mothers were well controlled for their glycemic state. They had 16% of babies with macrosomia while in our study, it was only 4.3%. This high incidence of macrosomia was attributed to high HbA1c levels of >8.5% which was seen in 58% of mothers. They also encountered congenital anomalies of which cardiac anomalies predominated with 94%. This again was attributed to uncontrolled diabetes.

Nurun *et al*. observed that hypoglycemia was detected till 6 h of life with lowest blood glucose value encountered at 2 h [10]. They suggested glucose monitoring in IDM only during the first 2 h of life which was not the case in our study. As per our study, if the GDM was well controlled, there were lesser chances of fetal morbidity and mortality which was also found in the case–control study done by González-Quintero *et al*. [11]. They compared fetal outcome in well-controlled GDM versus suboptimal controlled and found higher incidence of macrosomic hypoglycemia, jaundice, and stillbirth in the suboptimally controlled GDM. We observed a significant correlation of neonatal hypoglycemia at maternal HbA1c >6.5. These results were in accordance with the study done by Mahapatra and Raj [12].

Mimouni *et al*. reviewed the pathophysiology and management of neonatal complication of diabetes in pregnancy and concluded that adequate maternal glycemic control before and during pregnancy was the best prevention of many potential problems of IDM [13]. This was similar to our study. The rate of hypoglycemia was 8% in the study conducted by Qadir *et al*. which did not match with our study [14]. Stenninger *et al*. found that even asymptomatic hypoglycemia may be a risk factor for impaired neurodevelopment and must, therefore, be identified, prevented, and treated [15]. This supports our study of the transmission of mother's glycemic control to newborn which acts as a screening test and thereby helps in preventing asymptomatic hypoglycemia and long-term neurologic dysfunction which can be as mild as learning disabilities to as major as seizures disorder in future life. Our study had a few limitations. It was a single-center study and the sample size was small.

CONCLUSION

Neonatal HbA1c correlates well with maternal HbA1c level after birth. Early detection of GDM by screening high-risk group and achieving good glycemic control antenatally will facilitate reduction in social and financial burden and also reduce morbidity and mortality in IDM.

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Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Edbor A, Chikkam K, Dua H. Correlation of glycemic control in newborn at birth to maternal glycemic control. Indian J Child Health. 2020; 7(3):98-100.

Doi: 10.32677/IJCH.2020.v07.i03.001