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Original Article

Incidence and Risk Factors of Neonatal Hypoglycemia During the First 48 Hours of Life in a Tertiary Level Hospital

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Abstract:

Neonatal hypoglycemia is one of the common metabolic problems causing neonatal mortality and neurodevelopmental impairments. In developing countries, where the classic risk factors for neonatal hypoglycemia prevail; understanding the prevalence and association of hypoglycemia in different settings is essential. Our aim of this study was to identify the incidence and associated risk factors that predicted the occurrence of neonatal hypoglycemia during the first 48 hours of life. This hospital-based prospective case-control study was undertaken in the Department of Pediatrics in Faridpur Medical College Hospital, Bangladesh; from June 1, 2019 to July 31, 2019. Blood glucose levels of all the admitted newborns were noted on two occasions at 24 hours apart. Hypoglycemic neonates were selected as case and 3 euglycemic neonates for each case with similar age and sex were selected as control. Clinical characteristics of the mother and the baby were analyzed statistically in relation to the occurrence of hypoglycemia. We have found the incidence of neonatal hypoglycemia was 17.2%. Prematurity, low birth weight, small and large for gestational age, perinatal asphyxia, hypothermia, and delay in the initiation of breast feeding were significant neonatal factors. Maternal factors such as gestational diabetes mellitus, eclampsia, and fever during delivery had strong association as well. Understanding the incidence and risk factors may help prompt identification of hypoglycemic baby may also help to take early and effective measures to prevent the sequels of neonatal hypoglycemia.

Key words: Neonatal hypoglycemia, Incidence, Risk factors.

Introduction:

Neonatal hypoglycemia is one of the common metabolic abnormalities encountered in neonatal medicine[1-3]. Soon after birth, from 3% to as much as 29% babies encounter hypoglycemic condition[4-7]. It occurs frequently as a transient disorder, particularly in premature and small-for-gestational-age infants and if not treated promptly, it may lead to significant neurologic consequences, such as seizures and permanent brain damage or death[4,6,8-12].

However, controversy exists regarding the definition and management of clinically significant neonatal hypoglycemia especially in asymptomatic patients[1,4,13,14]. Also, the reported incidence usually varies with the defined glucose level for neonatal hypoglycemia, population, glucose measurement technique and feeding schedule[15].

In developing countries, established risk factors of neonatal hypoglycemia such as low birth weight, hypothermia, and delay in the onset of breast feeding are common. Moreover, hypoglycemia is surprisingly common even in apparently full term babies in these countries[16,17]. Neonatal deaths are unequally distributed worldwide, with approximately 98% occurring in the developing countries[18-20]. However, simple low-cost interventions can help to reduce the incidence of neonatal death even in countries with limited resources[21,22].

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As screening the blood glucose of all the babies is not feasible in resource-poor set-up, identifying the risk factors of neonatal hypoglycemia is critical to find out the infants 'at risk' in order to reduce their morbidity and mortality by appropriate timely intervention.

Our purpose of this study was to identify the incidence of hypoglycemia and to find out antepartum, intrapartum, and neonatal factors that are associated with neonatal hypoglycemia during the first 48 hours of life.

Materials and Methods:

It was a hospital based prospective case-control study undertaken in the Department of Pediatrics in Faridpur Medical College Hospital, Bangladesh. Venous blood was sent to the hospital laboratory of all the admitted newborns in the Department of Pediatrics from June 1, 2019 to July 31, 2019 on two occasions at 24 hours apart for random blood sugar estimation by glucose oxidase method in an autoanalyzer.

By 31 July 2019, a total of 186 newborns were admitted, among them 32 neonates were hypoglycemic. For each of the detected hypoglycemic cases, 3 euglycemic neonates with similar age and sex were selected as control and a total of 128 neonates were enrolled in the study. For every baby in the sample population, relevant antenatal, natal and postnatal information was documented. Logistic regression of the multiple variables and Pearson's Chi-square test of independence was performed to test the clinical characteristics of the mother and the baby in relation to the occurrence of hypoglycemia. Univariable conditional logistic regression analyses were carried out for each possible explanatory variable and those with a significance of $p<0.05$ were retained for inclusion in the saturated models.

Based on recent studies, 2.2 mmol/L was chosen as the low normal value for blood glucose[1,12,15,23,24]. All babies detected to have hypoglycemia (blood glucose level <2.2 mmol/L) were treated promptly as per the hospital protocol.

Prior to data collection, ethical clearance was obtained from the ethical committee of Faridpur Medical College Hospital.

Results:

Out of 186 admitted newborns, 32 (17.2%) were found to be hypoglycemic. Twenty three babies developed hypoglycemia during the first day of life and 3 had hypoglycemia throughout the first two days in spite of the treatment.

Table I shows the clinical characteristics of the mother with the result of chi-square analysis. Nearly one-third of the mothers had a BMI >25 kg/m^2 at the time of delivery. Mother with gestational diabetes mellitus showed a significant association with neonatal hypoglycemia. On the other hand, oligohydramnios and eclampsia were also found to have relation in the development of neonatal hypoglycemia.

Table I: Distribution of patients according to clinical characteristics of the mother (n=128)

Traits	Number of cases	Hypoglycemia	p value
BMI at delivery ≥25 kg/m^2	40	19	0.03
Gestational diabetes mellites	6	5	<0.001
Parity			
Primigravida	68	14	0.76
Multigravida	60	18	0.83
Oligohydramnios	15	4	0.02
Eclampsia	7	5	0.01

Table II depicts the delivery characteristics in relation to the development of hypoglycemia. From the analysis, prolonged second stage of labour, maternal fever during delivery as well as induced and assisted vaginal delivery were found to be related to neonatal hypoglycemia.

Table II: Distribution of patients according to delivery characteristics (n=128)

Traits	Number of cases	Hypoglycemia	p value
Induced labour	20	10	0.05
Prolonged second stage of labour	30	13	0.01
Maternal fever during delivery	5	3	0.01
Mode of delivery			
Normal vaginal	90	17	0.87
Assisted vaginal delivery	5	2	0.04
Caesarean section	33	13	0.36

The clinical characteristics of the neonates are summarized in table III. Large (LGA) or small (SGA) for gestational aged babies were at greater risk of developing hypoglycemia. Although the majority of the

babies were born at term, among the preterm babies, a significant portion had hypoglycemia. Hypothermic neonates also had a significant relation to the development of hypoglycemia. At the same time, babies with birth weight <2500 gm, birth asphyxia and those who got their first breastfeeding more than 2 hours later, had also increased the risk of developing hypoglycemia.

Table III: Distribution of patients according to clinical characteristics of the infants (n=128)

Traits	Number of cases	Hypoglycemia	p value
Intrauterine growth			
SGA	16	13	<0.001
LGA	7	5	<0.001
Gestational age			
Preterm	31	17	<0.001
Term	97	15	
Birth weight			
<2500 gm	51	21	0.02
≥2500 gm	77	7	
Birth asphyxia	30	18	0.02
Hypothermia	28	20	<0.001
Time of first breastfeeding			
≤2 hours	71	10	
>2 hours	57	22	0.01

SGA - Small for gestational age, LGA - Large for gestational age.

Results of the univariable analysis were used to select candidate variables for the development of saturated model displayed in table IV.

Table IV: Results of univariable conditional logistic regression analyses for variables associated with neonatal hypoglycemia

Variable	OR (95% Cl)	p value
Maternal characteristics		
BMI at delivery >25 kg/m^2	0.98 (0.68-1.20)	0.03
Gestational diabetes mellitus	1.32 (0.66-1.51)	<0.001
Oligohydramnios	0.80 (0.58-1.13)	0.02
Eclampsia	1.11 (0.80-3.87)	0.01
Delivery characteristics		
Induced labour	1.08 (0.51-1.32)	0.05
Prolonged second stage of labour	1.02 (0.46-1.14)	0.01
Maternal fever during delivery	1.92 (1.56-8.02)	0.01
Assisted vaginal delivery	1.30 (0.90-1.92)	0.04
Infant characteristics		
SGA	1.94 (0.88-2.02)	<0.001
LGA	1.76 (0.55-1.94)	<0.001
Preterm	2.44 (1.02-5.88)	<0.001
Birth weight <2500 gm	1.35 (1.11-4.67)	0.02
Birth asphyxia	0.95 (0.70-1.26)	0.02
Hypothermia	1.24 (0.65-2.48)	<0.001
First breastfeeding >2 hours after birth	0.88 (0.48-1.08)	0.01

Discussion:

Of the total sample population of 128, 32 babies had hypoglycemia during the first 48 h of life. The incidence of neonatal hypoglycemia at FMCH was 17.2% during the study period, an observation with reports from similar centres of the developing world[16,17]. A majority of the neonates (71.9%) developed hypoglycemia during the first day of life.

Gestational diabetes mellitus and maternal BMI at delivery were found to play a significant role in the development of hypoglycemia in our study. Other studies had also found significant relationship among these variables[3,4,12,15]. Also, we have seen relationship between eclampsia and neonatal hypoglycemia in our study. Sasidharan et al also found association of hypoglycemia with complicated hypertensive disorders of pregnancy[16].

Although some studies have not found any association of oligohydramnios with the development of neonatal hypoglycemia, we have found that this variable was related to the development of hypoglycemia in our population[4,12]. A study done in India by Sasidharan et al have also found relation to hypoglycemia with oligohydramnios[16].

In our study, we found maternal fever during labour or prolonged second stage of labour were more common with hypoglycemia (p = 0.01). Maternal fever during delivery has also been found to have significance in a study by DePuy et al[4]. We also found induced labour or assisted vaginal delivery have a relationship with neonatal hypoglycemia. Sasidharan et al and others have also found influence of hypoglycemia with these factors in their studies[16].

We have found a strong relationship of hypoglycemia with the SGA or LGA babies. These relationship have been addressed in many studies done previously[3,15,16,25-27]. Preterm, hypothermic babies or babies with birth asphyxia in our study had suggestive association with hypoglycemia. Other studies done worldwide have also found correlation of these conditions with the development of neonatal hypoglycemia[4,15,25,27,28]. Birth weight <2500 gm or breastfeeding the baby >2 hours later after birth had also important impact on hypoglycemia in our study. Other studies done by Depuy et al, Duvanel et al also support these variables for their connection with neonatal hypoglycemia[4,12,29]. Several reports showed that blood glucose level can increase after feeding in case of transient hypoglycemia[30]. It suggests that timely feeding after birth can also reduce the incidence of neonatal hypoglycemia.

Conclusion:

Hypoglycemia is surprisingly common among neonates in developing countries. However, simple low-cost measures such as proper antenatal and delivery care along with early feeding especially for low birth weight infants, or those having disproportionate growth can significantly reduce the prevalence of neonatal hypoglycemia.

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