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 sequelae of neonatal hypoglycemia.

Key words: Neonatal hypoglycemia, Incidence, Risk factors.

Introduction:

Neonatal hypoglycemia is one of the common metabolic abnormalities encountered in neonatal medicine¹-³. Soon after birth, from 3% to as much as 29% babies encounter hypoglycemic condition⁴-⁷. 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 death⁸⁻¹².

However, controversy exists regarding the definition and management of clinically significant neonatal hypoglycemia especially in asymptomatic patients¹³⁻¹⁵. Also, the reported incidence usually varies with the defined glucose level for neonatal hypoglycemia, population, glucose measurement technique and feeding schedule¹⁵.

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 countries¹⁶⁻¹⁷. Neonatal deaths are unequally distributed worldwide, with approximately 98% occurring in the developing countries¹⁸⁻²⁰. However, simple low-cost interventions can help to reduce the incidence of neonatal death even in countries with limited resources²¹⁻²².
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.

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/m² 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 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.

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

| Traits                        | Number of cases | Hypoglycemia | p value |
|-------------------------------|-----------------|--------------|---------|
| BMI at delivery ≥25 kg/m²     | 40              | 19           | 0.03    |
| Gestational diabetes mellitus | 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: 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.

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 world16-17. 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 variables1-3,12,15 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 pregnancy16.

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 population4,12. A study done in India by Sasidharan et al have also found relation to hypoglycemia with oligohydramnios4.

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 al4. 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 studies16.
We have found a strong relationship of hypoglycemia with the SGA or LGA babies. These relationship have been addressed in many studies done previously. 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. Several reports showed that blood glucose level can increase after feeding in case of transient hypoglycemia. 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.

References:
1. Cornblath M, Hawdon JM, Williams AF, Aynsley-Green A, Ward-Platt MP, Schwartz R, et al. Controversies regarding definition of neonatal hypoglycemia: Suggested operational thresholds. Pediatrics 2000; 105(5):1141-5.
2. Rozance PJ. Update on neonatal hypoglycemia. Curr Opin Endocrinol Diabetes Obes. 2014; 21(1):45-50.
3. Puchalski ML, Russell TL, Karlsen KA. Neonatal Hypoglycemia: Is There a Sweet Spot? Crit Care Nurs Clin North Am. 2018; 30(4):467-80.
4. DePuy AM, Coassolo KM, Som DA, Smulian JC. Neonatal hypoglycemia in term, nondiabetic pregnancies. Am J Obstet Gynecol. 2009; e45-e51.
5. Johnson TS. Hypoglycemia and the full-term newborn: how well does birth weight for gestational age predict risk? J Obstet Gynecol Neonatal Nurs. 2003; 32(1):48-57.
6. Alkalay AL, Sarnat HB, Flores-Sarnat L, Simmons CF. Neurologic aspects of neonatal hypoglycemia. Israel Medical Association Journal 2005; 7:188-92.
7. Stark J, Simma B, Blassnig-Ezeh A. Incidence of hypoglycemia in newborn infants identified as at risk. J Matern Neonatal Med. 2019; 27:1-6.
8. Sperling MA, Menon RK. Differential diagnosis and management of neonatal hypoglycemia. Pediatric Clinics of North America 2004; 51:703-23.
9. Hume R, McGeechan A, Burchell A. Developmental disorders of glucose metabolism in infants. Child Care Health Dev. 2002 Sep; 28(SUPPL. 1):45-7.
10. Hawdon JM. Hypoglycaemia and the neonatal brain. European Journal of Pediatrics 1999; 158 Suppl 1:S9-S12.
11. Menni F, De Lonlay P, Sevin C, Touati G, Peign C, Barbier V, et al. Neurologic outcomes of 90 neonates and infants with persistent hyperinsulinemic hypoglycemia. Pediatrics 2001; 107(3):476-9.
12. Duvanel CB, Fawer CL, Colling J, Hohlfeld P, Matthieu JM. Long-term effects of neonatal hypoglycemia on brain growth and psychomotor development in small-for-gestational-age preterm infants. J Pediatr. 1999; 134(4):492-8.
13. Cornblath M, Ichord R. Hypoglycemia in the neonate. Semin Perinatol. 2000; 24(2):136-149.
14. Rozance PJ. Update on neonatal hypoglycemia. Curr Opin Endocrinol Diabetes Obes. 2014; 21(1):45-50.
15. Kumar P, Saini, SS. An update on neonatal hypoglycemia. https://www.intechopen.com/books/hypoglycemia-causes-and-occurrences/an-update-on-neonatal-hypoglycemia. Accessed May 29, 2019.
16. Sasidhara CK, Gokul E, Sabitha S. Incidence and risk factors for neonatal hypoglycemia in Kerala, India. Ceylon Med J. 2004; 49(4):110-3.
17. Pal DK, Manandhar DS, Rajbhandari S, Land JM, Patel N, De L Costello AM. Neonatal hypoglycemia in Nepal I. Prevalence and risk factors. Arch Dis Child Fetal Neonatal Ed. 2000; S2(1):F46-F51.
18. Mitra DK, Mullany LC, Harrison M, Mannan I, Shah R, Begum N, et al. Incidence and risk factors of neonatal infections in a rural Bangladeshi population: a community-based prospective study. J Health Popul Nutr. 2018 Mar; 37(1):6.
19. Liu L, Hill K, Oza S, Hogan D, Chu Y, Cousins S, et al. Levels and Causes of Mortality under Age Five Years. Dis Control Priorities, Third Ed. Reprod Matern Born Newborn, Child Heal. 2016; 2-71-83.
20. Oestergaard MZ, Inoue M, Yoshida S, Mahanani WR, Gore FM, Cousins S, et al. Neonatal mortality levels for 193 countries in 2009 with trends since 1990: A systematic analysis of progress, projections, and priorities. PLoS Med. 2011; August 8(8):e1001080.
21. Barria RM. Introductory Chapter: Essential Issues in Neonatal Care. In: Selected Topics in Neonatal Care. InTech; 2018.
22. Ehret DY, Patterson JK, Bose CL. Improving Neonatal Care: A Global Perspective. Clinics in Perinatology 2017; 44:567-82.
23. Harris DL, Weston PJ, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. J Pediatri. 2012; 161(5):787-91.
24. Harris DL, Weston PJ, Battin MR, Harding JE. A survey of the management of neonatal hypoglycaemia within the Australian and New Zealand Neonatal Network. J Paediatr Child Health. 2014 Oct; 50(10):E55-62.
25. Jonas D, Dietz W, Simma B. Hypoglycemia in newborn infants at risk. Klin Padiatr. 2014; 226(6):287-91.
26. Adamkin DH, Papile LA, Baley JE, Bhutani VK, Carlo WA, Kumar P, et al. Clinical report - Postnatal glucose homeostasis in late-preterm and term infants. Pediatrics. 2011 Mar; 127(3):575-9.
27. Schaefer-Graf UM, Rossi R, Bühler C, Siebert G, Kjos SL, Dudenhausen JW, et al. Rate and risk factors of hypoglycemia in large-for-gestational-age newborn infants of nondiabetic mothers. Am J Gyneco. 2002; 187:913-7.
28. Sweet CB, Grayson S, Polak M. Management Strategies for Neonatal Hypoglycemia. J Pediatri Pharmacol Ther. 2013; 18(3):199-208.
29. Sinclair JC, Bottino M, Cowett RM. Interventions for prevention of neonatal hyperglycemia in very low birth weight infants. Cochrane Database Syst Rev. 2011; 10:CD007615.
30. Zhou W, Yu J, Wu Y, Zhang H. Hypoglycemia incidence and risk factors assessment in hospitalized neonates. J Matern Neonatal Med. 2015 Mar 1; 28(4):422-5.