

FREQUENCY AND CLINICAL CHARACTERISTICS OF SYMPTOMATIC HYPOGLYCEMIA IN NEONATES

Inayatullah Khan, Taj Muhammad, Muhammad Qasim Khan

Department of Child Health, Lady Reading Hospital and Khyber Teaching Hospital, Peshawar, Pakistan

ABSTRACT

Background: Hypoglycemia in neonates is associated with an increased risk of morbidity and mortality. The objective of this study was to determine the frequency and clinical characteristics of symptomatic hypoglycemia in neonates.

Methodology: This cross-sectional study was conducted at Department of Pediatrics & Neonatology, Lady Reading Hospital Peshawar, from April 2009 to March 2010. A total of 150 neonates with signs and symptoms of hypoglycemia were admitted. Gestational age, birth weight and clinical features were recorded on questionnaire. Blood glucose level was checked and any value less than 40mg/dl was considered as hypoglycemia. Data was analyzed by SPSS version 11.

Results: Out of 150 symptomatic neonates, 44(29.3%) were found to be hypoglycemic. Hypoglycemia was more common in males 34(32.7%) as compared to females 10(21.7 %), $p=0.04$, and was more frequent in first seven days of life 40(31.7%) than late neonatal age 4(16.6%), $p=0.04$. Hypoglycemia was present in 12(34%) small-for-gestational age, 31(30%) appropriate-for-gestational age and 1(8.3%) in large-for-gestational age babies ($p>0.05$). Hypoglycemia was seen in 11(32.3%) preterm and 33(29%) term babies ($p>0.05$). Feeding difficulty was the most common symptom of hypoglycemia 32(72.7%) cases followed by jitteriness in 28(62.7%) cases.

Conclusion: Symptomatic neonatal hypoglycemia is more common in male babies and in the early neonatal age. Blood glucose estimation is mandatory in neonates with signs and symptoms of hypoglycemia.

KEY WORDS: Neonate, Hypoglycemia, Neonatal hypoglycemia.

INTRODUCTION

Neonatal hypoglycemia is one of the most frequently encountered metabolic abnormalities in newborn infants. Its importance has been greatly emphasized especially in relation to acute neurological dysfunction as well as long term neurodevelopment impairment.¹⁻⁴ Estimates of the incidence of hypoglycemia in the newborn depends both on the definition of the condition and the methods of measurement. The overall incidence of hypoglycemia in newborn has been estimated as 1.3-5/1000 live births. The incidence has been found to be higher in developing countries & this may be attributed to large proportion of low birth weight or intrauterine growth retarded (IUGR) babies and improper feeding / nursing practices.^{5,6}

The symptomatic response of neonate to low blood glucose is variable with non-specific clinical features including pallor, feeding difficulties, tachypnea, hypotonia, abnormal cry, jitteriness, apnea, coma and convulsions. Hypoglycemia can

also be present without any apparent symptoms the so called "asymptomatic hypoglycemia" found in neonates at risk of hypoglycemia.⁷⁻¹⁰

Very limited data is available from Pakistan especially about the symptomatic neonates.

This study was aimed to know the frequency of hypoglycemia in symptomatic neonates and also to determine the common clinical characteristics of hypoglycemia in neonates. By early identification of hypoglycemia, the short term as well as long term morbidity can be decreased.

MATERIAL AND METHODS

It was a cross sectional study conducted at the Department of Paediatrics and Neonatology Post Graduate Medical Institute Lady Reading Hospital Peshawar from April 2009 to March 2010. All singleton neonates with signs and symptoms of hypoglycemia (seizures, jitteriness, lethargy, reluctant to feed, respiratory distress, hypotonia, hypothermia, abnormal cry, apnea and poor respiratory effort) presenting within 24 hours of birth

were admitted in Neonatology department of PGMI Lady Reading Hospital Peshawar. Newborns with gross dysmorphism and those who presented after 24 hours of birth without documentation of gestational age and birth weight were excluded. Patients were further assessed after taking informed consent from parents or relatives. Detailed history and clinical examination was carried out and relevant data was collected on pre-designed questionnaire. Blood was collected from peripheral vein through aseptic technique and was sent to the laboratory for blood glucose measurement, total serum calcium, serum electrolytes (Na, K) and complete blood count. Blood cultures and cerebrospinal fluid samples were also collected based on clinical suspicion. Moreover, selected babies were also evaluated by doing x-ray chest and echocardiography. Any blood glucose value less than 40 mg/dl (2.2mmol/l) was considered as hypoglycemia. Hypoglycemic neonates were treated with I.V glucose as per standard recommendations⁷. Blood glucose level was measured every 6 hourly in hypoglycemic babies. Hypoglycemic babies with clinical suspicion of birth asphyxia and/or neonatal sepsis were treated with I.V glucose. In case of improvement with glucose, symptoms were considered due to hypoglycemia. If babies remained symptomatic in spite of repeated normal glucose level then symptoms were attributed to birth asphyxia and/or neonatal sepsis. Babies were categorized as SGA (birth weight less than 10th centile), AGA (birth weight between 10th to 19th centile) and LGA (birth weight >90th centile) based on fetal growth charts¹¹. Gestational age (recorded as completed weeks) was assessed from maternal last menstrual period (LMP), ultra-

sound scan in the first trimester and Dubowitz examination results¹². Birth weight was measured without clothes and recorded in decimal of kilograms. Neonates were classified as pre-term (<37 weeks gestation), term (37 to 42 weeks) and post term (> 42 weeks). Jitteriness was defined (as opposed to seizures) as non-jerky, stimulus sensitive fine movements that ceases on grasping the hands and not accompanied by abnormal ocular phenomenon.

Data was entered in computer by using SPSS version 11. Mean \pm SD was calculated for birth weight and age of babies (in days). Frequencies as percentages are presented for gender, gestational age (preterm, term and post-term) and clinical characteristics. Chi-square test and independent sample t-test was used to compare gender, gestational age groups, birth weight categories and age of babies for significance of hypoglycemia. A p-value <0.05 was considered significant.

RESULTS

Mean age of our study population was 5+4.65 days and birth weight 2.8 \pm 0.86 kg. Out of 150 symptomatic neonates, 29.3% were found to be hypoglycemic. Hypoglycemia was more common in male as compared to female babies (32.7% vs 21.7%, p=0.04). Similarly hypoglycemia was more frequent in first seven days of life than late neonatal age (31.7 % vs 16.6 %, p=0.04). Symptomatic hypoglycemia was more common in preterm than term babies (32.3% vs 28.9%), although this was not statistically significant. SGA babies were at increased risk of hypoglycemia than AGA babies (34% vs 30%) or LGA babies (34%

Table 1: Characteristics of neonates with hypoglycemia.

	Hypoglycemia			p-value
		Yes	No	
Gender				
Male	104(69.3)	34(32.7)	70(67.3)	0.04
Female	46(30.7)	10(21.7)	36(78.3)	
Gestational age(wk)				
Preterm	34(22.7)	11(32.3)	23(67.7)	0.6
Term	114(76)	33(29)	81(71)	
Post-term	2(1.3)		2(100)	
Weight for gestational age				
Small for gestational age	35(23.2)	12(34.2)	23(65.8)	0.2
Appropriate for gestational age	103(68.7)	31(30)	72(70)	
Large for gestational age	12(8)	1(8.3)	11(91.7)	
Age of neonate				
1-7 days	126(84)	40(31.7)	86(68.3)	0.04
>7 days	24(16)	4(16.6)	20(83.4)	

Table 2: Signs and symptoms of hypoglycemic neonates. (n=44)

Signs/symptoms	Number (%)
Difficulty with breast feeding	32(72.7)
Jitteriness	28(62.7)
Seizures	16(37.3)
Respiratory distress	15(34)
Lethargy	13(30)
Hypotonia	12(27.3)
Hypothermia	11(26.7)
Abnormal cry	09(20)
Apnea	08(17.3)
Poor respiration	06(14)

vs. 8.3 %) which was statistically insignificant (Table 1).

Feeding difficulty was the most common symptom of hypoglycemia present in 72.7 % neonates followed by jitteriness in 62.7% cases and poor respiratory effort (14%). These findings are depicted in table 2.

Out of remaining 106 study cases with normal blood glucose (70.7%), sepsis was the most common diagnosis in 40 cases (26.8 %), followed by birth asphyxia in 32 cases (21.3%), hypocalcemia in 15 cases (10%), RDS in 7 cases (4.7%), congenital heart disease in 5 cases (3.3%), meningitis in 2 cases (1.3%), drug overdose in 2 cases (1.3%) and transient tachypnea of newborn in 3 cases (2.2%).

DISCUSSION

Hypoglycemia in neonates remains a common problem. The association of low blood glucose concentrations and abnormal development has prompted extensive research into the anticipation, clinical presentation and treatment of neonatal hypoglycemia. Various local, regional and international studies have been conducted but still many issues remain unsettled especially in developing countries.

Our study confirmed the high frequency of hypoglycemia in neonates especially with signs and symptoms. This high frequency could be because of more prevalent risk factors for hypoglycemia in our population including preterm births, intrauterine growth retardation, sepsis and perinatal asphyxia. The frequency of hypoglycemia in symptomatic neonates was 29.3 % in our study. These findings are consistent with those of Lodhi et al who reported hypoglycemia in 29.1%

neonates.¹³ They included babies who presented within 06 hours of birth and with known risk factor for hypoglycemia. Infants of diabetic mother were excluded in their study. In contrast to their methods, blood glucose of all symptomatic babies was measured in laboratory in our study. In a study conducted in Kenya, 23 % of neonates were hypoglycemic.¹⁴ Dashti et al reported 15.1 % prevalence of hypoglycemia while Shams et al reported the frequency of hypoglycemia as 3.5%.^{15,16} Similarly Sasidharan CK and colleagues reported an incidence of hypoglycemia in 4.1% neonates.¹⁷ The other study conducted in Turkey reported an incidence of neonatal hypoglycemia in 9.18% neonates.¹⁸ These differences may be due to variable definition of hypoglycemia, inclusion criteria, sample size and detection method of hypoglycemia.

Males were affected more than females in our study (32.7% vs 21.7%, $p=0.04$). Similar results have also been reported in a local study conducted by Hamid H and Chishti AL.⁶ Bell JJ also reported male predominance in 169 infants (100 males, 69 females).¹⁹ In contrast to our results, a local study by Lodhi MA et al has reported female predominance (199 female and 148 male).¹³

The risk of hypoglycemia is increased in premature, small for gestational age newborns and neonates born to diabetic mothers. In our study, hypoglycemia was more common in preterm as compared to term babies although the difference was not statistically significant. Burdan DR et al also reported more preterm babies as hypoglycemic than term babies (52.8% Vs 45.53%)²⁰. Hypoglycemia was present in 8.3% large for gestational age babies in our studies. These findings are consistent with those of Burdan DR et al.²⁰

The literature refers to numerous clinical features with low plasma glucose concentration. In our study, we found difficulty in feeding as the most common clinical presentation (72.7 %). Dashti et al also reported refusal of feeding as the most frequent symptom (45%).¹⁵ Other two clinical features were tremor and seizures. Almost all studies from local and international literature reported these observations with more or less similar percentages as reported in our study.^{13, 15- 17, 19, 20}

We found increased incidence of hypoglycemia in early neonatal age (84%). Lucas A et al & Maayan-Metzger A et al also reported increased hypoglycemia episodes in early neonatal age.^{21, 22} This could be explained on the basis of the fact that newborn glucose levels fall to a low point in the first 1-2 hours of life and then increased and stabilize gradually. Moreover, the risk factors also expose the neonate more to hypoglycemia in the early neonatal period. The number of days on

which hypoglycemia occurs is strongly related to reduced mental and motor development scores even after adjustment for a wide range of factors known to influence development.

Besides this useful information, our study has some limitations. As sample size was based on non-probability convenience sampling method, so these newborns may not be true representative of population. This calls for further studies with more robust statistical methods. Another limitation is the lack of important clinical parameters such as different feeding types (breastfeeding, formula or a combination of the two), different volumes per feed and different time intervals between feedings. All these factors might affect the glucose concentration. Moreover, it would have been interesting if babies were also assessed for hypoglycemia in the first few hours of birth.

CONCLUSION

Hypoglycemia is common in neonates especially in the first week of life. It is more common in male babies. Babies with signs and symptoms should have mandatory blood glucose screening.

Based on our study, we recommend high index of suspicion for hypoglycemia for early detection, prompt management and better outcome.

REFERENCES

1. Srinivasan G, Pildes RS, Cattamanchi G, Voora S, Lilien LD. Plasma glucose values in normal neonates: a new look. *J Pediatr* 1986; 109: 114-17.
2. Cornblath M, Reisner SH. Blood glucose in the neonate and its clinical significance. *N Engl J Med* 1965; 273: 378-81.
3. Rozance PJ, Hay WW. Hypoglycemia in newborn infants: features associated with adverse outcomes. *Biol Neonate* 2006; 90: 74-86.
4. Burns CM, Rutherford MA, Boardman JP, Cowan FM. Patterns of cerebral injury in neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics* 2008; 122: 65-74.
5. Wilker RE. Hypoglycemia and hyperglycemia in: Cloherty JP, Eichenwald EC, Stark AR. *Manual of neonatal care* 5th ed. Philadelphia. Lippencott Williams and Wilkins 2004: s569-78.
6. Ahmad H, Chishti AL. Neonatal hypoglycemia: an underreported entity in high-risk neonates. *Pak Pediatr J* 2000; 24: 9-11.
7. Sperling MA, Menon RK. Differential diagnosis and management of neonatal hypoglycemia. *Pediatr Clin N Am* 2004; 51: 703-23.
8. Memon S, A Memon MM. Spectrum and immediate outcome of seizures in neonates. *J Coll Physicians Surg Pak* 2006; 16: 717-20.
9. Kalhan S, Peter-Wohl S. Hypoglycemia: what is it for the neonate? *Am J Perinatol* 2000; 17: 11-14.
10. Moore AM, Perlman M. Symptomatic hypoglycemia in otherwise healthy breastfed newborns. *Pediatrics* 1999; 103: 837.
11. Lubchencho L, Hansman C, Dressler M, Boyd E. Intrauterine growth as estimated from liveborn birth weight data at 24 to 42 weeks gestation. *J Pediatr* 1962; 32: 793-800.
12. Dubowitz L, Dubowitz V, Goldberg C. Clinical assessment of gestational age in the newborn infants *J Pediatr* 1970; 77: 1-10.
13. Lodhi MA, Shah NA, Shabir G. Risk factors associated with neonatal hypoglycemia. *Professional Med J* 2006; 16: 687-90.
14. Osier FH, Berkley JA, Ross A, Sanderson F, Mohammed S, Newton CR. Abnormal blood glucose concentrations on admission to a rural Kenyan district hospital: prevalence and outcome. *Arch Dis Child* 2003; 88: 621-5.
15. Dashti N, Einollahi N, Abbasi S. Neonatal hypoglycemia: prevalence and clinical manifestations in Tehran Children's Hospital. *Pak J Med Sci* 2007; 23: 340-3.
16. Shams S, Akhtar MN, Anwar CM. Neonatal hypoglycemia. *Pak Armed Forces Med J* 1997; 47: 7-10.
17. Sasidharan CK, Gokul E, Sabitha S. Incidence and risk factors for neonatal hypoglycaemia in Kerala, India. *Ceylon Med J* 2004; 49: 110-3.
18. Dalgic N, Ergenekon E, Soysal S, Koç E, Atalay Y, Gücüyener K. Transient neonatal hypoglycemia—long-term effects on neurodevelopmental outcome. *J Pediatr Endocrinol Metab* 2002; 15: 319-24.
19. Bell JJ, August GP, Blethen SL, Baptista J. Neonatal hypoglycemia in a growth hormone registry: incidence and pathogenesis. *J Pediatr Endocrinol Metab* 2004; 17: 629-35.
20. Burdan DR, Botiu V, Teodorescu D. Neonatal hypoglycemia. The incidence of the risk factors in Salvator VUIA Obstetrics-Gynecology Hospital, ARAD. *TMJ* 2009; 59:77-80.
21. Lucas A, Morley R, Cole TJ. Adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia. *BMJ* 1988; 297: 1304-8.
22. Maayan-Metzger A, Lubin D, Kuint J. Hypoglycemia Rates in the first days of Life among term Infants born to Diabetic Mothers. *Neonatology* 2009; 96: 80-85.

Corresponding author:

Dr. Taj Muhammad
Department of Child Health
Khyber Teaching Hospital
Peshawar, Pakistan
E-mail: dr.tajmahsud2000@gmail.com