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Original Research Article

The incidence of asymptomatic hypoglycemia in term newborn babies weighing more than two kilograms

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ABSTRACT

Background: Neonatal hypoglycemia is a common metabolic problem especially in cases like prematurity, sepsis and small gestational age. Episodes of asymptomatic hypoglycemia may occur due to many risk factors. The present study aimed to evaluate the incidence of asymptomatic hypoglycemia in term new born babies weighing more than 2 kg, to study the plasma sugar level at various time points during first 48 hours of life and to study the effect of maternal factors like parity, mode of delivery, glucose infusion during labour, and time since last feed on plasma sugar level.
Methods: A hospital based longitudinal study was conducted over a period of one year from April 2005 to March 2006 in Kilpauk Medical College Hospital, Chennai. 400 babies born of consecutive deliveries were included in the study. Their plasma glucose levels were assessed in cord blood, 3 hr, 12 hr and 36 hr of life. Plasma glucose levels were analysed with regards to distribution, variables like parity, mode of delivery, dextrose infusion during labour and time since last feed. The plasma glucose levels were statistically analysed by paired student 't' test, multiple analysis of variance (ANOVA), chi- square test using SPSS (version 7.5) statistical package.
Results: The overall incidence of hypoglycemia was seen in 20% of the neonate's in which 29.7% in small gestational age (SGA) and 16.7% in appropriate gestational age (AGA) babies. A significant ($p < 0.01$) association between hypoglycemia and birth weight was observed. The association between hypoglycemia with parity, mode of delivery, sex of the baby and glucose infusion received by the mother was studied, but no significant association was found. A significant difference in plasma glucose based on birth weight at 3rd hour, 12th hour and 36th hour was observed ($p < 0.05$). None of the infants showed any clinical signs of hypoglycemia.
Conclusions: The incidence of hypoglycemia was noted in 20% of the neonates. Low birth weight was considered as risk factor. A significant association was also observed between plasma glucose, mode of delivery and time since last fed.

Keywords: Birth weight, Maternal factors, Neonatal hypoglycemia, Plasma glucose level

INTRODUCTION

Hypoglycemia is a common metabolic problem seen in newborn period.[1] Blood glucose levels are frequently lower in newborn babies than in older children due to inadequate liver stores and impaired gluconeogenesis and glycogenolysis.[2] The significance needs to be interpreted based on infant's size, gestation and clinical condition as well as availability of energy sources and ongoing energy demands. Classically these states occur in small for

gestational age infants (SGA) (weight less than 10th percentile), large for gestational age infants (LGA) (weight more than 90th percentile), infant of diabetic mother and preterm infants.

Hypoglycemia in neonates can be symptomatic and asymptomatic. The incidence of asymptomatic hypoglycemia in Term appropriate for gestational age babies was found to vary between 12-14%.[3,4]

Symptomatic hypoglycemia presents with non-specific features like jitteriness, apathy, episodes of cyanosis, convulsions, apneic spells, weak or high pitch cry, limpness (or) lethargy, difficulty in feeding and hypothermia.[5]

Both symptomatic and asymptomatic hypoglycemia were found to be associated with adverse long term neurodevelopmental outcome as shown by lower head circumference and developmental scores.[6-8] Hence early diagnosis and treatment of hypoglycemia should be our goal, as glucose is the main source of energy for brain especially in the first few days of life.

The aim of the present study was to determine the incidence of asymptomatic hypoglycemia in term new born babies weighing more than 2kg, to study the plasma sugar level at various time points during first 48 hours of life and to study the effect of maternal factors like parity, mode of delivery, glucose infusion during labour, and time since last feed on plasma sugar level.

METHODS

This longitudinal study is conducted over a period of one year from April 2005 to March 2006 in Kilpauk Medical College Hospital, Chennai.

400 newborn babies born of consecutive deliveries were included in the study. All term newborn babies weighing, more than 2kg and exclusively breastfed were included in the study.

Exclusion criteria were neonates with respiratory distress, perinatal asphyxia, meconium aspiration syndrome polycythemia (capillary PCV >70) and neonates receiving antibiotics or admitted in newborn ward, neonates born to mother with hypertension, diabetes mellitus, anaemia and neonates with congenital anomalies. All the mothers were explained about the study and informed consent was obtained from them. All infants were exclusively breastfed.

Infants delivered by caesarean section were started on breast feeds as soon as the mother was transferred to ward. Babies delivered by labour natural were fed as soon as possible. No prelacteal feeds were given. Ethical clearance was obtained from the institutional ethical committee.

Maternal details like parity, mode of delivery, dextrose infusion during labour and time since last feed at the time of sampling were recorded in a proforma. Sex of the baby, birth weight and gestational age were also recorded. Term gestation was defined as 37-42 weeks based on new Ballard's score. Birth weight was defined as appropriate or small for gestational age based on Usher's chart.

Collection of sample

Venous blood was collected, centrifuged at 12,000 rpm for 10 minutes and plasma glucose was evaluated within 15 minutes by glucose oxidase method using semiautonalyser in biochemistry lab. The cohorts were followed up and their plasma glucose were assessed in cord blood, 3, 12 and 36 hours of life, these time points were chosen to study the most vulnerable period of glucose homeostasis.

Plasma glucose levels were analysed with regards to distribution, variables like parity, mode of delivery, dextrose infusion during labour and time since last feed. Lethargy, Jitteriness and convulsions alleviated by bolus of IV glucose were considered to be clinical signs of hypoglycemia. Neonates were considered asymptomatic if low plasma glucose were not associated with clinical signs. Neonates found to have low plasma glucose were clinically examined, given additional breastfeed and plasma glucose reassessed after 30 minutes.

Infants who continued to be hypoglycemic inspite of adequate feeds were excluded and managed as per standard protocol for asymptomatic hypoglycemia. Infant who became symptomatic for hypoglycemia were also excluded and treated according to standard protocol. The babies who had asymptomatic hypoglycemia were registered in high risk newborn clinic of our hospital and are being followed up for neurodevelopmental sequelae. The plasma glucose levels were statistically analysed by paired student 't' test, multiple analysis of variance (ANOVA), chi- square test using SPSS (version 7.5) statistical package.

RESULTS

Four hundred neonates including 101 small for gestation (SGA) and 299 appropriate for gestation (AGA) were involved in the study after meeting requirements of inclusion criteria. Of them 190 were males and 210 were females. There were 171 primiparous and 229 multiparous mothers were involved in the study.

Out of 400, 146 were delivered by normal vaginal route and 22 mothers of them received dextrose infusion. 100 were born through assisted deliveries and 154 were through caesarean section. Among them, 32 and 100 mothers had received dextrose infusion respectively.

Table 1: Demographic and clinical characteristics of the neonates.

Variables	Number	%
Weight		
Small for gestation	101	25.3
Appropriate for gestation	299	74.8
Sex		
Male	190	47.5
Female	210	52.5
Parity		
Primi	171	42.8
Multi	229	57.3
Mode		
Normal	146	36.5
Assisted	100	25.0
Caesarean	154	38.5
Hypoglycemia		
Absent	320	80
Present	80	20

Table 2: Mothers who received dextrose infusion.

Dextrose	Delivery					
	Normal		Assisted		Caesarean	
	No.	%	No.	%	No.	%
Received	22	15	32	32	100	64
Not received	124	85	68	68	54	36

The overall incidence of hypoglycemia was seen in 20% of the neonates. In maximum cases (45.6%) hypoglycemia was noted at 3rd hour after birth followed by 36 hours of age (28.8%). Evidence of hypoglycemia was not seen after 48 hours of age.

Table 3: Incidence of hypoglycemia at different ages.

Various ages	Number	%
Cord blood	23	15.4
3rd hour	68	45.6
12th hour	15	10.2
36th hour	43	28.8

Among the 101 SGA and 249 AGA neonates 30 and 50 cases had hypoglycemia respectively with significant difference between the two cases (p <0.01).

Of 121 cases of normal deliveries 25 neonates born with hypoglycemia. Out of 80 assisted deliveries 20 neonates had hypoglycemia and 119 cases of caesarean deliveries 35 neonates were diagnosed of having hypoglycemia. Amongst the171 primiparous mothers, 34 neonates had hypoglycemia. Among neonates born to 229 multiparous mothers, 46 had hypoglycemia. 45% of neonates were born with hypoglycemia among 154 mothers who had dextrose infusion before delivery.

Out of 156 male neonates, 34 had hypoglycemia and among 164 females, 46 neonates were having hypoglycemia.

Table 4: Association of hypoglycemia with various factors.

Factors	Hypoglycemia				P value
	Absent		Present		
	No.	%	No.	%	
Weight					
SGA	71	71.3	30	29.7	P <0.01
AGA	249	83.3	50	16.7	
Type of delivery					
Normal	121	37	25	31	
Assisted	80	25	20	25	P >0.05
Caesarean	119	28	35	44	
Parity					
Primi	137	42.8	34	43	P
Multi	183	57.3	46	57	>0.05
Dextrose infusion					
Received	118	36.8	36	45	P
Multi	202	63.2	44	55	>0.05
Sex					
Male	156	48	34	42	P
Female	164	52	46	58	>0.05

Plasma glucose concentrations were recorded at different age groups as show in Table 5.

Mean plasma glucose values in cord blood was found to be 75.61 with SD of 25.81. It was higher compared to other blood samples at different age groups. The plasma glucose gradually rises to mean value of 56.78 mg at 12th hour and attained a stable value of 61.64 at 36th hour so there is a significant variation in plasma sugar during the first 48 hours of life as shown by repeated analysis of variance.

Table 5: Plasma glucose concentration at 4 different ages.

Duration	Mean	Median	S.D.	P value
Cord Blood	75.61	70	25.81	
3rd hour	48.62	46	11.94	P <0.01
12th hour	56.78	56	11.68	
36th hour	61.64	60	11.95	

Comparison of plasma sugar at various age groups based on weight of the neonates was given in Table 6. The mean blood glucose values in both SGA babies were lower compared to AGA babies at 3rd, 6th and 12th hours after delivery (p<0.05). No significant association was noted in cord blood between the two cases.

The influence of maternal factors like parity, mode of delivery on plasma glucose level was tabulated in Table 7 and Table 8. No significant association was observed between plasma glucose and parity of mother.

The mean plasma glucose values of both parities were almost similar. The mean blood glucose in cord blood was higher in caesarean and induced deliveries than in normal delivery.

A rebound fall in plasma glucose level is noted in this group compared to normal delivery at 3rd hour of life but was raised significantly at 12 and 36 hours in all delivery cases.

Table 6: Comparison of plasma glucose at various ages based on weight.

Plasma glucose	Parity	N	Mean	S.D.	't'	P value
Cord blood	Small	101	75.76	33.34		
	Appropriate	299	75.66	22.77	0.069	>0.05
3rd hour	Small	101	41.11	10.133		
	Appropriate	299	51.17	11.442	7.854	<0.05
12th hour	Small	101	52.60	11.34		
	Appropriate	299	63.96	12.44	7.454	<0.05
36th hour	Small	101	54.70	9.425		
	Appropriate	299	63.98	11.823	7.156	<0.05

Table 7: Comparison of plasma glucose in infant born to primiparous and multiparous women.

Plasma glucose	Parity	N	Mean	S.D.	't'	'P'value
Cord blood	Primi	171	76.06	25.990	0.304	>0.05
	Multi	229	75.27	25.731		
3rd hour	Primi	171	47.66	11.694	1.400	>0.05
	Multi	229	49.35	12.102		
12th hour	Primi	171	57.36	11.576	0.849	>0.05
	Multi	229	56.35	11.770		
36th hour	Primi	171	61.39	12.023	0.358	>0.05
	Multi	229	61.88	11.929		

Table 8: Comparison of plasma glucose based on mode of delivery.

Delivery		Plasma glucose			
		Cord blood	3rd hour	12th hour	36th hour
Normal	Mean	62.61	51.02	57.60	62.72
	S.D.	18.032	12.854	11.453	12.364
Assisted	Mean	83.10	47.26	56.97	58.80
	S.D.	29.032	9.771	11.588	10.026
Caesarean	Mean	83.07	47.25	55.89	62.46
	S.D.	25.101	12.044	11.970	12.483
	P value	<0.01	<0.01	<0.05	<0.02

Table 9: Comparison of plasma glucose at different time intervals.

Plasma glucose at different intervals				
Mean	S.D.	't' Value	P value	
Cord blood	75.61	25.812	12.606	<0.01
12th hour	56.78	11.683		
Cord blood	75.61	25.812	9.720	<0.01
36th hour	61.64	11.956		
3rd hour	48.63	11.944	11.538	<0.01
12th hour	56.78	11.683		
3rd hour	48.63	11.944	30.526	<0.01
36th hour	61.64	11.956		

Comparison of plasma glucose concentration at different time intervals was given in Table 9. The plasma glucose concentration was significantly higher in cord blood compared to 12 hour and 36-hour blood samples.

The plasma glucose at 12 hour was significantly raised compared to 3rd hour blood sample.

The plasma glucose level in relation to time since last feed was presented in Table 10. Breast feeding was initiated at the earliest possible time after delivery in all neonates. The plasma glucose concentration was significantly lower (<0.001) in babies who were unfed till 3 hours after their birth. In 127 neonates breast feeding was initiated within 1 hour and in 124 patients it was initiated within 2 hours of their birth. Their plasma glucose level was raised significantly at 12 and 36 hours.

Table 10: Plasma glucose in relation to time since last feed.

Time since last feed	3rd hour	12th hour	36th hour
Unfed			
No.	169	0	0
Mean	46.99		
S.D.	12.046		
Upto 1 hour			
No.	127	109	100
Mean	51.03	55.48	63.20
S.D.	11.034	10.243	10.835
Upto 2 hours			
No.	104	195	171
Mean	52.12	57.28	62.28
S.D.	11.08	11.44	11.28
Upto 3 hours			
No.	0	85	105
Mean		56.68	61.19
SD		13.37	13.645
Upto 4 hours			
No.		11	24
Mean	0	61.64	52.54
SD		14.767	9.532
P value	<0.001	<0.01	<0.01

DISCUSSION

The incidence of hypoglycemia clearly varies with definition chosen, population studied (post-natal age, gestation age and weight for gestational age).[9,10] The earliest marker for predicting hypoglycemia in first few hours of life would be cord blood sugar.[5] The maximum risk for hypoglycemia is in first 24 hours and definitely not after 72 hours except, in persistent hypoglycemia due to rare causes like inborn errors of metabolism and hyperinsulinism.

Asymptomatic and symptomatic hypoglycemia in small for gestation babies may produce adverse effect on brain growth and psychomotor development which may range from subtle learning disability to severe sequelae.[11] Hence, early initiation of breastfeeding and frequent breastfeeding will prevent hypoglycemia in newborn babies.

The present study population comprised of 400 term newborn babies weighing more than 2 kg and born of various modes of delivery like normal vaginal delivery, caesarean section and assisted delivery. The mean birth weight of the study population was 2750 g ranging from 2.1 kg to 3.9 kg. About one third of the study population was SGA babies (101). Female preponderance was seen in the study. This is similar to the study done by Samayam et al.[12]

A higher incidence of hypoglycemia was seen in neonates delivered by multiparous mother (57%) against neonates delivered to the primiparous mother (43%). But in a study conducted by Samayam et al in 100 neonates, higher incidence of hypoglycemia was seen in neonates in delivered to primi mothers (23.07%).[12]

According to Sasidharan et al, hypoglycaemia was a common problem in asymptomatic normal neonates. In addition to this they found that breast feeding delay of greater than 2 hours and maternal oligihydraminos after delivery considerably increases the risk of neonatal hypoglycemia.[13] The overall incidence of asymptomatic hypoglycemia was in the present study was found to be 20%. Diwakar et al in their study of healthy term infants found out the incidence to be 14%.[14] In our study, the incidence among AGA babies was 16.7% which is comparable to Heck et al.[15] The incidence among SGA babies in our study was 29.7%. Narang in a similar study of SGA babies found out the incidence to be 25.2%.[16]

The incidence of hypoglycemia in blood samples taken at various times was studied. In that the 3rd hour sample showed the maximum incidence of hypoglycemia (17%). This may be attributed to the maximum fall in blood sugar level at 3rd hour of life. The lowest incidence was noted at 12th hour of life (10.75%). All the babies were asymptomatic and hypoglycemia was corrected on breast feeding and rechecking sugar level after 1 hour.

In this study, the relationship between hypoglycemia and birth weight was analysed using chi-square test and have found a strong relationship between two factors. This data was agreed with the data of previous studies.[17,18]

The association between hypoglycemia with parity, mode of delivery, sex of the baby and glucose infusion received by the mother was studied, but no significant association was found. Diwakar et al in his study also concluded that no association was found between hypoglycemia and parity or mode of delivery.[14]

The plasma glucose concentration was also studied over a period of 48 hours on cord blood, 3rd hr, 12th hour and

36th hour samples. The mean plasma glucose was higher in cord blood compared to other samples. This may be due to large number of mothers (154) of them receiving dextrose infusion during labour. There is a fall in mean plasma glucose at 3rd hour of life this may be explained by delay in feeding of babies till 3 hours and maximum fall in plasma glucose occurs at 3 hours of age. Srinivasan et al in his study of plasma glucose in term neonates noted maximum fall in plasma glucose at 2nd hour of life.[19]

The plasma glucose was analysed at various ages based on birth weight and found a significant difference in plasma glucose based on birth weight at 3rd hour, 12th hour and 36th hour. Narang et al in a similar study showed maximum incidence of low blood glucose in small for gestation babies within first 24 hours.[16] The influence of maternal factors like parity, mode of delivery on plasma glucose level was also studied, but no significant association was noted between them. The plasma glucose level in relation to time since last feed was also studied and observed an association between them, that is in unfed babies the mean plasma glucose was found to be low and also in babies who were last fed more than 3-4 hours at the time of sampling. But Diwakar et al did not find any association in his study.[14] Anderson et al also observed a high incidence of hypoglycemia in babies who were unfed (or) were delayed breast feeding upto 24 hours.[20]

None of the infants who had low plasma glucose levels showed any clinical signs of hypoglycemia. However, the glucose level in all increased immediately after feed. This was also noted by Hoseth et al, Hawdon et al and Diwakar et al in their studies.[3,4,14] The ability of neonatal brain to use alternative fuels like ketone bodies may ensure the infant to be symptom free. This was extensively studied by Hawdon et al but he also remarked that metabolic substrates other than glucose may play important role only after 48-72 hours of life, until that glucose continues to be the major source of energy supply to brain.[4]

CONCLUSION

The study shows an incidence of asymptomatic hypoglycemia in 20% of neonates in which 29.7% in SGA and 16.7% in AGA babies. This concludes that there was a significant association between birth weight and hypoglycemia. Results also assumed significant association between plasma glucose, mode of delivery and time since last fed. Hence babies of such categories need a continuous plasma glucose monitoring and management in order to reduce the infant mortality and neuro-developmental sequel in later life.

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REFERENCES

1. Dhananjaya CD, Kiran B. Clinical profile of hypoglycemia in newborn babies in a rural hospital setting. Int J Biol Med Res. 2011;2(4):1110-4.
2. Stanley CA, Baker L. The causes of neonatal hypoglycemia. (Editorial) N Engl J Med. 1999;340(15):1200-1.
3. Hoseth E, Joergensen A, Ebbesen F, Moeller M. Blood glucose level in a population of healthy breastfed term infants of appropriate size for gestationalage. Arch Dis child Fetal Neonatal Ed. 2000;83:227-9.
4. Hawdon JM, Ward Platt MP. Metabolic adaptation in small for gestational age infants. Arch Dischild 1993;68:262-8.
5. Williams AF. Hypoglycemia of the newborn. Rev Bull World Health organization. 1997;75:261-90.
6. Duvanel CB, Fawer CL. Long term effect of neonatal hypoglycemia on brain growth and psychomotor development in small for gestational age infants. J Paediatrics. 1999;134:492-8.
7. Lucas A, Morley R, Cole TJ. Adverse neurodevelopmental outcome of moderate ultimated hypoglycemia. BMJ. 1988;297:1304-8.
8. Behrman RE, Nelson KR. Textbook of Paediatrics. 16th Edn. 2000: 533-534.
9. Sexson WR. Incidence of neonatal hypoglycemia: A matter of definition. J Pediatr. 1984;105:149–50.
10. Harris DL, Weston PJ, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. J Pediatr. 2012;161:787-91.
11. Alkalay Arie L. Brain Imaging Findings in Neonatal Hypoglycemia: Case Report and Review of 23 Cases. Clinics of Pediatrics (Phila). 2005;44(9):783-90.
12. Samayam P, Ranganathan PK, Kotari UD, Balasundaram R. Study of Asymptomatic Hypoglycemia in Full Term Exclusively Breastfed Neonates in First 48 Hours of Life. J Clin Diagn Res. 2015;9(9):7-10.
13. Sasidharan CK, Gokul E, Sabitha S. Incidence and risk factors for neonatal hypoglycemia in Kerala, India. Ceylon Med J. 2004;49(4):110-3.
14. Diwakar KK, Sasidhar MV, Plasma glucose level in term infants who are appropriate size for gestation and exclusively breastfed. Arch Dis. Child FetalNeonatal Ed. 2002;87:46-8.
15. Erenburg H. Serum glucose level in breastfed and bottle fed infants during 48 hours of life. Arch Dis child. 1992;64:1486-8.
16. Narang A, Bhat MA, Kumar P. Hypoglycemia in small for gestational age babies. Ind J Paediatr. 2001;68 (10):963-5.
17. Scholl TO, Chen X, San Khoo C, Lenders C. The dietary glycemic index during pregnancy: influence on infant birth weight, fetal growth, and biomarkers of carbohydrate metabolism. Am J Epidemiol. 2004;159(5):467-74.

18. Weissman A, Solt I, Zloczower M, Jakobi P. Hypoglycemia during the 100-g oral glucose tolerance test: incidence and perinatal significance. Obstet Gynecol. 2005;105(6):1424-8.
19. Srinivasan G, Pildes RS, Cattamanchi G, Vooras, Lillen Lb. Plasma glucose values in term neonates: A new look. J Pediatrics. 1986; 109114-7.
20. Anderson S, Shakya KN, Shrestha LN, Costello AM. Hypoglycaemia: a common problem among uncomplicated newborn infants in Nepal. J Trop Pediatr. 1993;39(5):273-7.

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