

HYPOGLYCAEMIC STATUS IN LOW BIRTH WEIGHT NEONATES DURING FIRST 48 HOURS OF LIFE.

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Abstract

Introduction: In developing countries more than 90% infants are born with low birth weight (LBW). In Bangladesh the incidence is about 30%. Newborn baby has got a definite difference in metabolic profile from the adult; this difference is much more pronounced in case of LBW newborn. Infants born prematurely or following intrauterine malnutrition may develop abnormally low plasma glucose concentration for a prolonged period as a result of the failure to adapt a metabolic and endocrine response.

Glucose is an essential nutrient for the brain. Abnormally low levels (hypoglycaemia) can cause encephalopathy and have the potential to produce long-term neurological injury. Adequate knowledge about neonatal physiology is important in the management of LBW neonates in the neonatal nursery specially in the first 48 hours of life as most of the neonatal deaths occur in this critical period of time.

Objectives: To evaluate the clinical features of hypoglycaemic low birth weight (LBW) neonates in the first 48 hours of life.

Methods: This cross-sectional study was conducted on 56 LBW neonates in the inpatient departments of Paediatrics and Obstetrics of Combined Military Hospital (CMH), Dhaka

between 15th September 2010 to 14th March 2011. LBW (Weight <2500gm) neonates, both term and preterm, from birth to 48 hours of age and who were well at the time of blood collection were included in this study. After enrollment of the newborn, with all aseptic precaution blood samples were taken from cord (as basal) at birth, from venous blood at 2 hours and then from capillary blood at 4 hours, in between 12-24 hours and in between 24-48 hours by heel prick from each case. Cord and capillary blood glucose were measured by using "Accu-Check-Active"- glucometer. Blood glucose concentrations less than 2.6 mmol/L irrespective of weight and gestational age were considered as low for the purpose of analysis.

Results: It was revealed from the study that the mean birth weight was 1.77 gm mean gestational age was 36.09 weeks. 30 (53.57%) were intrauterine growth retarded (IUGR) and 26 (46.43%) were appropriate for gestational age (AGA). Out of thirty IUGR, 24 (51.79%) infants had low blood glucose (<2.6 mmol/L) levels. Twenty-two (75.86%) of 29 low birth weight infants showed low blood glucose at one of the five time points, 07 (17.07%) had low values on two hypoglycemia at 12-24 hours of age.

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The mean blood glucose concentration in LBW infants were 4.03 mmol/L at birth (cord), 2.33mmol/L at 2 hours, 2.96mmol/L, at 4 hours 3.14mmol/L, at 12—24hours and 3.43mmol/ L at 24—48hours of age. In the first 48 hours, the lowest blood glucose (mean) concentrations were found at 2 hours after delivery.

Hypoglycaemia was most common among the preterm intrauterine growth retarded (IUGR) neonates at 2 hours after delivery. Most 23 (79.31%) of the hypoglycaemic infants were asymptomatic and 6 (20.69%) had symptoms.

Early feeding prevents hypoglycaemia and appears to influence subsequent glucose values. Among the manifestations jitteriness, hyperalert, tachypnoea, high pitched cry, lethargy, apnoea and poor feeding were observed.

Conclusion: The study findings may be helpful in the management of LBW neonates with hypoglycaemia and will encourage the mother in initiation of feeding immediately after delivery.

Key-Words: Low birth weight, Hypoglycaemia, Neonate.

Introduction

More than 95% of LBW babies are born in developing countries. In Bangladesh about 30 percent of infants are born with low birth weight¹. It has been known for long that the newborn baby has got a definite difference in metabolic profile from the adult. This difference is much more pronounced in case of LBW newborn.

About 39% of the death occurred in infants weighing less than 1500gm at birth and born at less than 32 weeks of gestation or both, half of those within the first 48 hours². At birth with sudden discontinuation of the nutrient supply from the mother, the neonates need adaptive response including mobilization of the glucose and fatty acid from the glycogen and triglycerides depots to meet the energy demands. Hypoglycaemia is a common disorder in neonates³. Infants born prematurely or following intrauterine malnutrition may develop abnormally low plasma glucose concentration for a prolonged period as a result of failure to adapt a metabolic and endocrine response^{4,5}.

One Malaysian study showed that hypoglycaemia was seen in 34.2% of small for gestational age (SGA) and in 27.1% of appropriate for gestational age (AGA) infants⁶. Glucose is an essential nutrient for the brain. Abnormally low levels (hypoglycaemia) can cause encephalopathy and have the potential to produce long-term neurological injury. The level at which this potential for long term injury is reached is controversial^{7,8}. The increased incidence of LBW makes such studies vital to formulation of recommendation for prevention and treatment within first 48 hours of life to reduce neonatal mortality rate⁹. Unfortunately, there has not been enough study on this topic. So an attempt has been made to evaluate the glycaemic status of the newborn babies with LBW and correlate it with data available from other countries.

Materials and Methods

This cross-sectional study was performed at the inpatient departments of Paediatrics and Obstetrics at Combined Military Hospital, Dhaka during 15th September 2010 to 14th March 2011.

LBW (Weight <2500gm) neonates both term and preterm, from birth to 48 hours of age and well at the time of blood collection were included in this study. LBW infants with any obvious illness, baby of diabetic, Impaired Glucose Tolerance (IGT) or Gestational Diabetic Mothers (GDM) and baby receiving intravenous infusion of glucose were excluded from the study. Data of the antenatal, natal and postnatal period of the enrolled baby and the mother were collected from mother, baby's attendant and the attending doctors using a predetermined questionnaire.

A total of 56 LBW neonates fulfilling the inclusion criteria at birth were recruited for this study. A detailed history was taken and thorough clinical examination was done in each case and information were recorded in the questionnaire. Septicaemia, hypothermia, perinatal asphyxia that may affect the glycaemic status as well as features of hypoglycemia were cautiously excluded from history and clinical examination. After enrollment of the newborn, with all aseptic precaution blood samples were taken from cord (as basal) at birth, from venous blood at 2 hours and then from capillary blood at 4 hours, in between 12-24 hours and in between 24-48 hours by heel prick from each case. Cord and capillary blood glucose were measured by using "Accu-Check-Active"- glucometer. After strict aseptic precaution venous blood was drawn from antecubital vein for second sample at 2 hours of age from each case and was sent to the laboratory as early as possible. As drawing of blood on five occasions in LBW neonates is very difficult, only 2nd sample was taken from venous blood at 2 hours of age from each case to measure plasma glucose. In addition, plasma glucose determination was immediately done if glucometer reading was <2.6 mmol/L. Efficacy of the glucometer was ascertained by compared the results of same sample done by both glucometer of colorimeter. All infants were fed with breast milk, expressed breast milk or formula milk after delivery. Maintenance feeding was given

hourly. The time of first feeding was recorded. Weight of the subject was taken using baby weighing scale machine. Gestational age was estimated from the obstetric history and New Ballard Score. Blood glucose concentrations were analyzed with regard to distribution, variations with age, and mode of delivery, gestational age, birth weight, and time of first feeding, IUGR Vs AGA, and preterm IUGR Vs term IUGR. Blood glucose concentrations less than 2.6 mmol/L irrespective of weight and gestational age were considered as low for the purpose of analysis. During follow up, the features such as jitteriness, irritability, tremors, lethargy, weak cry, high pitch cry, apnoea, poor feeding, vomiting, convulsion, hyperalertness, sweating, tachypnoea alleviated by a bolus of intravenous 10% dextrose (2ml/kg) were considered to be clinical signs of hypoglycaemia. Neonates were considered as asymptomatic if low blood glucose concentrations were not associated with clinical signs.

Data Analysis

Unpaired students 't' test and repeated analysis of variance were applied where necessary for statistical analysis using the SPSS (12-version) statistical package.

Results

A total of 56 LBW (<2500gm) neonates were included in this study; the mean birth weight was 1.77 gm (range 1.22kg—2.4kg), mean gestational age was 36.09 weeks (range 30—40 weeks). 30 (53.57%) were intrauterine growth retarded (IUGR) and 26 (46.43%) were appropriate for gestational age (AGA). Out of thirty IUGR 24 (80%) were term IUGR and 6 (20%) were preterm IUGR. 24 (42.86%) infants were born vaginally and 32 (57.14%) were delivered by lower segment caesarean section. The mean blood glucose concentration in LBW infants were 4.03 mmol/L (range 2.56 mmol/L—5.28mmol/L) at birth (cord), 2.33mmol/L (range 1.78—3.44mmol/L) at 2 hours, 2.96mmol/L (range 1.89—3.89mmol/L) at 4 hours,

3.14mmol/L (range 1.78—5.61mmol/L) at 12—24hours and 3.43mmol/L (range 2.78—5.67mmol/L) at 24—48hours of age. In the first 48 hours, the lowest blood glucose (mean) concentration were found at 2 hours after delivery and the level gradually increased with increasing postnatal

Age. Line diagram showing blood glucose level of low birth weight babies in first 48 hours of life according to sampling time (Fig-1).

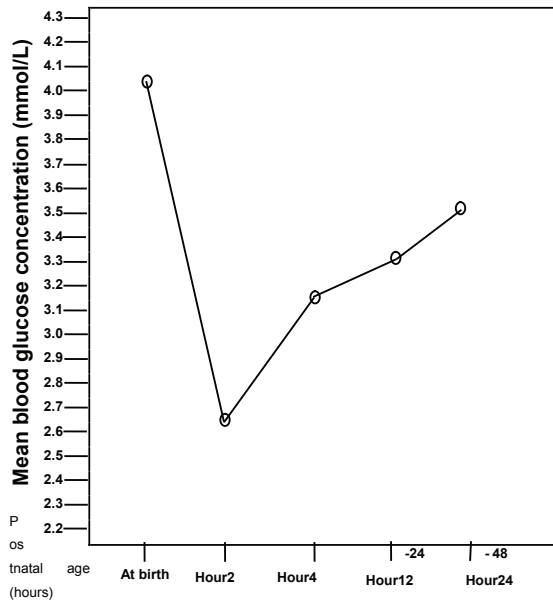


Fig-1: showing mean blood glucose concentration of LBW neonates increasing with increasing postnatal age.

Repeated analysis of variance showed significant difference between blood glucose levels at birth (cord blood), at 2 hours, 4 hours, 12-24 hours and 24-48 hours of age (p=0.005) (Table-I).

Table-I: Blood glucose levels (mmol/L) in LBW neonates at 5 different times in first 48 hours of life (n=56).

Age (hours)	Mean±SD of blood glucose (mmol/l)	Median blood glucose (mmol/l)	Range of blood glucose (mmol/l)	Interquartile range	SEM
At birth	4.03±0.61	4.17	2.56-5.28	4.5-3.7	0.081
2	2.33±0.35	2.22	1.78-3.44	2.5-2.1	0.047
4	2.96±0.38	2.94	1.89-3.89	3.2-2.8	0.051
12-24	3.14±0.51	3.17	1.78-5.61	3.4-3.0	0.069
24-48	3.43±0.56	3.39	2.78-5.67	3.6-3.3	0.075

Repeated analysis of variance, p=0.005

The mean blood glucose concentration in LBW infants were 4.03 mmol/L (range 2.56 mmol/L—5.28mmol/L) at birth (cord), 2.33mmol/L (range 1.78—3.44mmol/L) at 2 hours, 2.96mmol/L (range 1.89—3.89mmol/L) at 4 hours 3.14mmol/L (range 1.78—5.61mmol/L) at 12—24hours and 3.43mmol/L (range 2.78—5.67mmol/L) at 24—48hours of age.

In the first 48 hours, the lowest blood glucose (mean) concentration were found at 2 hours after delivery and the level gradually increased with increasing postnatal age (Figure-1). Repeated analysis of variance showed significant difference between blood glucose levels at birth (cord blood), 2 hours, 4 hours, 12-24 hours and 24-48 hours of age (p=0.005) (Table-I).

There was statistically significant difference seen in blood glucose levels of low birth weight neonates with variation of birth weight at 2 and 4 hours of age (Table-II).

Table-II: Blood glucose (mmol/L) distribution according to birth weight (n=56).

Birth weight	At birth	2 h	4h	1224 h	2448 h
<1.6 kg					
n	13	13	13	13	13
Mean	4.09	2.11	2.36	2.8	3.45
SD	0.48	0.26	0.29	0.43	0.71
SE	0.13	0.07	0.08	0.12	0.19
1.6-2 kg					
n	19	19	19	19	19
Mean	4.13	2.48	2.90	3.31	3.61
SD	0.07	0.09	0.10	0.15	0.64
SE	0.07	0.09	0.10	0.15	0.16
>2.0 kg					
n	24	24	24	24	24
Mean	3.95	2.45	3.35	3.13	3.46
SD	0.76	0.39	0.36	0.37	0.37
SE	0.15	0.08	0.07	0.08	0.08
P Value	0.80	0.04	0.04	0.13	0.66

Among the 56 low birth weight neonates, 29 (51.79%) infants had low blood glucose (<2.6 mmol/L) levels. Twenty-two (75.86%) of 29 low birth weight neonates showed low blood glucose at one of the five time points, 07 (17.07%) had low values on two occasions. Out of 56, 29 had hypoglycaemia at 2 hours, 4 had hypoglycemia at 4 hours and 3 had hypoglycemia at 12-24 hours of age. Hypoglycaemia was not found at birth and at 24-48 hours of age (Table-III).

Table-III: Frequency of hypoglycaemia at different sampling times (n=56)

Time of sampling	Blood Glucose	
	<2.6 mmol/L (%)	≥2.6 mmol/L (%)
At birth (cord)	0 (0)	56 (100)
2	29 (51.79%)	27 (48.31%)
4	04 (8.93%)	52 (91.07)
12-24	03 (7.14)	53 (92.86)
24-48	0 (0)	56(100)

Out of 29 hypoglycemic LBW infants, 23 (79.31%) had no symptoms and 6 (20.96%) had symptoms. There was no statistically significant (p>0.05) difference between blood glucose levels of symptomatic and asymptomatic hypoglycaemic LBW neonates in the first 48 hours of age (Table-IV).

Table-IV: Hypoglycaemia among the low birth weight babies (n=29) with or without symptoms.

Hypoglycemia	Total no of case	Frequency of hypoglycaemia (mmol/L)	Frequency of hypoglycaemia (mmol/L)	Range of blood Glucose	Mean±SD of Blood glucose (mmol/L)	P value
Asymptomatic	29	23	79.31%	1.89-2.5	2.18±0.18	>0.05
Symptomatic	29	6	20.69%	1.78-2.5	1.97±0.27	

Statistical analysis was done by unpaired t test

Study showed blood glucose levels of hypoglycaemic preterm IUGR, term IUGR and preterm AGA, were 66.66%, 62.50% and 38.46% respectively in the first 48 hours of age (Table-V).

Table-V: Hypoglycaemia among preterm IUGR, term IUGR and the preterm AGA babies.

	Total no of case	Frequency of hypoglycaemia (mmol/L)	Frequency of hypoglycaemia (mmol/L)	Range of blood glucose (mmol/L)	Mean±SD of blood glucose (mmol/L)	P Value
Preterm IUGR	6	4	66.66%	1.73-2.11	1.91±0.14	0.42
Term IUGR	24	15	62.50%	2.11-2.5	2.6±0.17	
Preterm AGA	26	10	38.46%	2.11-2.5	2.17±0.17	

Statistical analysis was done by repeated analysis of variance

There was no statistically significant difference among the blood glucose levels of hypoglycemic preterm IUGR, term IUGR and preterm AGA neonates in the first 48 hours of age (Table-V).

There was statistically significant difference seen between the blood glucose levels of hypoglycemic early feed group (48%) and later fed group (54.84%) neonates (Table-VI).

Table-VI: Hypoglycaemia among the early fed group and later fed group.

Hypoglycemia	Total no of case	Frequency of hypoglycaemia (mmol/L)	Percentage of hypoglycaemia (mmol/L)	Range of blood glucose (mmol/L)	Mean±SD of blood glucose (mmol/L)	P value
Early fed Group	25	12	48.00	2.11-2.5	2.4±0.16	<0.05
Later fed Group	31	17	54.84	1.8-2.28	2.08±0.16	

Early fed group=First feeding started within 30 minutes of delivery

Later fed group=First feeding started after 30 minutes of delivery (Range 30 minutes to 2.5 hours).

No statistically significant difference was found between the blood glucose levels of infants born by caesarean section and normal vaginally delivery during the first 48 hours of life (Table-VII).

Table-VII: Comparison of blood glucose (mmol/L) in LBW neonates born by caesarean section (n=32) and those delivered vaginally (n=24).

Age (Hours)	Mode of delivery	Mean±SD of blood glucose (mmol/L)	SE	P Value
At birth (cord)	Caesarean	4.04±0.58	0.102	0.397
	Vaginal	3.90±0.63	0.129	
2	Caesarean	2.27±0.32	0.057	0.251
	Vaginal	2.37±0.36	0.073	
4	Caesarean	3.05±0.40	0.070	0.075
	Vaginal	2.85±0.43	0.087	
12-24	Caesarean	3.02±0.47	0.084	0.114
	Vaginal	3.25±0.58	0.118	
24-48	Caesarean	3.49±0.58	0.103	0.679
	Vaginal	3.55±0.57	0.117	

There was no statistically significant difference between the blood glucose levels of infants born by caesarean section and normal vaginally delivery during the first 48 hours of life (Table-VII).

Whereas statistically significant (p>0.040) difference was seen between the blood glucose levels of preterm IUGR and term IUGR at 2 hours of delivery (P>0.040) (Table-VIII).

Table-VIII: Comparison of blood glucose (mmol/L) levels between preterm IUGR (n=6) and term IUGR (n=24).

Age (hours)	Preterm Vs Term IUGR	Mean±SD of blood glucose (mmol/L)	SE	P Value
At birth (cord)	Preterm IUGR	3.99±0.32	0.132	0.760
	Term IUGR	3.91±0.70	0.144	
2	Preterm IUGR	2.12±0.22	0.089	0.040
	Term IUGR	2.37±0.26	0.054	
4	Preterm IUGR	2.88±0.48	0.196	0.740
	Term IUGR	2.94±0.38	0.078	
12-24	Preterm IUGR	3.21±0.33	0.135	0.126
	Term IUGR	2.97±0.47	0.096	
24-48	Preterm IUGR	3.35±0.43	0.177	0.595
	Term IUGR	3.48±0.55	0.112	

There was statistically significant difference between the blood glucose levels of preterm IUGR and term IUGR at 2 hours of delivery (P>0.040) (Table-VIII).

Among the features of hypoglycaemia in 6 symptomatic cases, jitteriness in 4 cases (66.66%), hyper alertness in 3 cases (50%), lethargy in 3 cases (50%), tachypnoea in 3 cases (50%), high pitched cry in 2 cases (33.33%), apnoea in 2 cases (33.33%) and poor feeding in 1 case (16.66%) were observed (Table-IX).

Table-IX: Clinical manifestations of hypoglycemia in low birth weight neonates in first 48 hours of life (n=6)

Features of hypoglycemia	No of patients n=6	Percent of patients (%)
Jitteriness	04	66.66
Hyper alertness	03	50.00
Tachypnoea	03	50.00
High pitched cry	02	33.33
Poor feeding	01	16.66
Lethargy	03	50.00
Apnoea	02	33.33

Statistical analysis was done by repeated analysis of variance.

Discussion

Almost 50 years after it was first described, neonatal hypoglycaemia remains a commonly encountered clinical problem. Although many authors deny that neonatal hypoglycaemia is a pathophysiological reality¹⁰. The relationship between hypoglycaemia and abnormal clinical signs was proven by rapid correction of the abnormality by intravenous glucose¹¹. This study showed that the mean blood glucose concentration (2.33mmol/L) was significantly lower at 2 hours after delivery than any other time point of first 48 hours of age and then the blood glucose levels gradually increased to reach normal levels with increasing postnatal age.

Srinivasan and voora observed that there was a decline in plasma glucose level during the first 2 hours of postnatal life followed by a rise, reaching a steady-state concentration by 2 to 3 hours after birth¹². In this study, it was observed that out of 56 LBW infants had blood glucose levels of less than 2.6 mmol/L in 1st 2 hrs of life but only 7 of those had the hypoglycaemic level continued in the 4 and 12-24 hours of age and require treatment.

Among the 29 hypoglycaemic LBW neonates, 23 (79.31%) had no symptoms and 6 (20.69%) had symptoms . Beard and Cornblath showed that 20% of the hypoglycaemic infants were symptomatic and the remaining 80 % of infants were asymptomatic¹³. This study also showed that there was no significant difference between blood glucose levels of symptomatic and asymptomatic hypoglycaemic LBW neonates in the first 48 hours of age.

The neurophysiological study of 5 neonates of varying birth weight and gestations by Koh also demonstrated no significant difference between blood levels of symptomatic and asymptomatic hypoglycaemic neonates¹⁴.

This study showed that hypoglycaemia was most common among preterm IUGR, (66.66%). It also showed significant difference between the blood glucose levels of early fed group and later fed group of LBW babies and early feeding influenced the subsequent blood glucose levels. Our study showed no significant difference between the blood glucose levels of neonates born by caesarean section and by normal vaginal delivery during the first 48 hours of life. One Indian study showed that blood glucose levels were lower in LBW neonates whose feeding were not given early¹⁵.

Beard showed that early feeding of newborn premature infants prevented hypoglycemia and influenced subsequent blood glucose levels¹³. Hawdon and Ward also showed similar results in a cross sectional study of 1546 term infants and 62 preterm infants^{16,17}. Srinivasan and Pildes showed that early feeding had been associated with a more rapid increase in blood glucose concentration after the immediate postnatal fall^{18,19}. So early feeding is an important determinant of blood glucose level in LBW neonates.

The present study showed statistically significant difference between blood glucose levels of preterm IUGR and term IUGR at 2 hours of delivery (P=0.040). Lubchencho and Bard also showed that preterm IUGR had a significantly lower mean blood glucose concentration in the first few postnatal hours than the term IUGR (p<0.05)¹³. Among the features of hypoglycaemia in 6 symptomatic cases jitteriness, hyper-alertness, tachypnoea , and lethargy were observed most commonly in our study. Pildes and Cornblath also observed that the common features of hypoglycaemia are jitteriness (56.4%), poor feeding (30.8%), lethargy (38.4%), irritability (10.2%) and convulsion²⁰ (20.5%).

Conclusion

In this study it was observed that birth weight had a positive correlation with blood glucose levels of LBW neonates in the first 48 hours of age. Lowest blood glucose concentrations were found at 2 hours after delivery. Most of the hypoglycaemic LBW infants were asymptomatic. Among the features of hypoglycemia observed in some neonates jitteriness, hyperalertness, tachypnoea and lethargy were most common. Early and frequent feeding prevents the early hypoglycaemic episodes and appears to influence subsequent glucose levels in low birth weight neonates.

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