



HYPOGLYCEMIA IN EXCLUSIVELY BREASTFED LOW BIRTH WEIGHT NEONATES

Paediatric Medicine

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ABSTRACT

Background and Aim: Hypoglycemia is an important problem encountered in Low Birth Weight (LBW) neonates. Incidence and risk factors associated with hypoglycemia in low birth weight neonates on exclusive breast milk were studied. **Material and Methods:** A Prospective observational study was done between Jan-June 2022. Low birth weight neonates (≥ 1.8 kg < 2.5 kg) who were fed exclusively with breast milk were screened for hypoglycemia by measuring capillary blood glucose by glucometer strips at 1, 2, 6, 12, 24, 48 and 72 hours of age. **Results:** 180 Low Birth Weight neonates were included in the study, of which 41 developed hypoglycemia with incidence of 22.7%. Majority of them (85.3%) were asymptomatic. 70.7% of hypoglycemia episodes occurred in first 24 hours of life. 58.5% neonates with hypoglycemia had only one episode while 31.7% and 9.8% had 2 and 3 or more episodes of hypoglycemia respectively. Incidence was more in Pre term (PT) (27.3%) compared to Full Term (FT) neonates (16.2%). Also Small for Gestational Age (SGA) neonates were more prone to hypoglycemia compared to Appropriate for Gestational Age (AGA) neonates (48.2% against 18.4%). Incidence in PT SGA, FT SGA and PT AGA neonates was 27.9%, 20.3 & 18.4% respectively. Incidence was also more in neonates born to primigravida mothers and those delivered by cesarean section. **Conclusion:** Low birth weight Neonates especially late preterms and SGA neonates on exclusive breast milk should be monitored for hypoglycemia in first 72 hours of life. Early initiation of breast feeding should be ensured to prevent hypoglycemia in them.

KEYWORDS

Neonatal Hypoglycemia, Low Birth Weight neonates.

INTRODUCTION

Hypoglycemia is one of the most common metabolic disorders in neonates and occurs due to inability to maintain normal glucose homeostasis. At the time of birth, the neonate is abruptly switched from a state of continuous supply of glucose from maternal blood through placental transfer to maintaining its own supply of glucose both during periods of fasting and in between fasting. Maintenance of normoglycemia in the newborn depends upon the adequacy of the glycogen stores, maturation of glycogenolytic and gluconeogenic pathways and an integrated endocrine response. Certain groups of neonates like Low Birth Weight (LBW) neonates, Preterm (PT), Small for Gestational Age (SGA), Large for Gestational Age (LGA), Infant of Diabetic Mother (IDM) and sick neonates are at increased risk of hypoglycemia.²

Hypoglycemia may be asymptomatic or symptomatic. The symptoms associated with hypoglycemia are nonspecific and include irritability, tremors, jitteriness, twitching, convulsions, refusal of feeds, lethargy and apnea.³ Severe hypoglycemia is a known risk factor for neuronal cell death and long term sequelae of hypoglycemia include mental retardation, recurrent seizure activity and poor neurodevelopmental outcome.^{4,5}

Studies have been done on hypoglycemia in various high risk groups of neonates. This study was designed to study the occurrence of hypoglycemia in exclusive breast fed low birth weight neonates. The aim of the study was to find the incidence of hypoglycemia in low birth weight neonates and also to find the risk factors associated with hypoglycemia in these neonates.

MATERIALS AND METHODS

This prospective observational study was conducted in the department of pediatrics of a tertiary care hospital in Ahmedabad, Gujarat between January 2022 to June 2022. The study was approved by the Institutional Ethical Committee. Inclusion criteria included all Low Birth Weight (LBW) neonates (≥ 1.8 < 2.5 kg) who were exclusively on breast milk either given directly or expressed and given with katori spoon. Neonates who were sick and admitted in NICU in first 72 hours of life for other illnesses like perinatal asphyxia, respiratory distress, sepsis etc. and those with major congenital malformations were excluded. Informed consent was taken from parents and details of neonate and mother were recorded in a predesigned proforma. Neonatal details like gender, birth weight, gestational age and maternal

details like gravida, mode of delivery and presence of maternal illness like Gestational Diabetes Mellitus (GDM), Pregnancy induced hypertension (PIH) etc. were noted. Problems of the neonates and examination findings were recorded.

Counselling for exclusive breast feeding was done in all the cases and feeding assistance given to all mothers following delivery. Breast milk was given either through direct feeding or by giving expressed milk with katori spoon. Breast feeding was ensured within 30 minutes of birth in cases of normal vaginal delivery and within 2 hours of LSCS. Thereafter, feeding was given every two to three hours including 2 to 3 night feeds.

Capillary blood glucose levels were monitored using glucometer reagent strips at 1, 2, 6, 12, 24, 48 and 72 hours of life and also at any time when symptoms suggestive of hypoglycemia occurred. Tremors, irritability, jitteriness, seizures, lethargy, poor feeding and apnea were considered as clinical signs of hypoglycemia. Neonates were considered asymptomatic if hypoglycemia was not associated with any clinical sign. Hypoglycemia was defined as capillary blood glucose < 40 mg/dl or plasma blood glucose < 45 mg/dl.¹

In neonates who were found to be hypoglycemic by glucometer measurement, hypoglycemia was confirmed by plasma glucose level using venous blood sample. Neonates with hypoglycemia were clinically examined, relevant investigations were sent and they were treated according to standard protocol. Neonates with asymptomatic hypoglycemia and those with blood glucose level > 25 mg/dl were given breast milk (directly or expressed) and blood glucose levels were measured after 1 hour. If glucose levels were still $> 25 < 40$ mg/dl, breast milk was given under observation and if breast milk secretion was inadequate formula feeds were given and blood glucose level rechecked after 1 hour. If the level was ≤ 25 mg/dl or if symptomatic hypoglycemia occurred, baby was admitted in NICU and treated with IV dextrose as per standard protocol.

Gestational age of neonates was assessed by date of Last Menstrual Period (LMP) and Modified New Ballard score. Neonates with gestational age < 37 weeks were considered preterm (PT) whereas those $\geq 37 < 41$ weeks were considered full term (FT) neonates. Those with gestational age 34⁰⁷ – 36⁶⁷ weeks were late preterm neonates. Intergrowth 21 charts were used to assess the weight for gestational age of the neonates.⁽⁶⁾ Those whose weight was less than 10th centile for

gestational age and gender were considered Small for Gestational Age (SGA) while those whose weight was between 10th to 90th centile were considered Appropriate for Gestational Age (AGA).

Statistical Analysis

The recorded data was compiled and entered in spreadsheet computer program (Microsoft Excel 2007) and was analysed and presented as frequency and percentage.

RESULTS

180 low birth weight neonates (≥ 1.8 kg < 2.5 kg) were included in the study. Of these, 118 (65.6%) were males while 62 (34.4%) were females. 106 neonates (58.9%) were late preterms while 74 (41.1%) were full term neonates. 109 neonates (60.6%) were delivered by normal vaginal delivery while 71 (39.4%) were delivered by LSCS. 93 neonates (51.7%) were born to primigravida mothers while 87 (48.3%) neonates were born to multigravida mothers. 142(78.9%) were SGA while 38 (21.1%) were AGA.

Out of the 180 LBW neonates studied, 41 developed hypoglycemia. The incidence of hypoglycemia was 22.7%. Of the 41 hypoglycemic neonates, 35(85.4%) were asymptomatic while 6 neonates (14.6%) were symptomatic. Jitteriness, lethargy, seizures and poor feeding were the clinical manifestations noted in the symptomatic neonates. 29 neonates (70.7%) developed the first episode of hypoglycemia in first 24 hours of life, 8 neonates (19.5%) on 2nd day of life and 4 (9.8%) on 3rd day of life. 24 (58.5%) neonates had only one episode of hypoglycemia while 13(31.7%) neonates had 2 episodes and 4 (9.8%) had 3 or more episodes.

Incidence of hypoglycemia in male neonates was 23.4% as against 21.7% in females. 21.1% neonates delivered vaginally developed hypoglycemia against 25.3% neonates delivered by LSCS. Neonates born to primigravida mothers had a higher incidence of hypoglycemia at 31.2% against 13.7% in neonates born to multigravida mothers. 23.4% neonates between ≥ 1.8 < 2.2 kg developed hypoglycemia against 21.7% neonates between ≥ 2.2 < 2.5 kg. Hypoglycemia was noted in 27.4% late preterms and 16.2% full term neonates. SGA neonates were more prone to develop hypoglycemia with an incidence of 48.2 % against 18.4% noted in AGA neonates. Incidence of hypoglycemia in PT SGA, FT SGA and PT AGA neonates was 27.9%, 20.3% and 18.4% respectively. Table 1 and Table 2 shows clinical characteristics and incidence of hypoglycemia of the study subjects.

Table 1: Clinical characteristics and incidence of hypoglycemia in LBW neonates

Characteristics		Number (%)N=180	Neonates with hypoglycemia(N=41) Number (%)	Incidence of hypoglycemia (%)
Birth Weight (kgs)	≥ 1.8 < 2.2	111 (61.7%)	26 (63.4%)	23.4%
	≥ 2.2 < 2.5	69 (38.3%)	15 (36.6%)	21.7%
Gestational Age (weeks)	34/0/7 to 36 6/7	106 (58.9%)	29 (70.7%)	27.4%
	$\geq 37/0/7$	74 (41.1%)	12 (29.3%)	16.2%
Birth weight + Gestational Age	SGA	68 (37.8%)	19 (46.3%)	27.9%
	PT SGA	74 (41.1%)	15 (36.6%)	20.3%
	FT SGA	74 (41.1%)	15 (36.6%)	20.3%
Gestational Age	AGA	38 (21.1%)	7 (17.1%)	18.4%
	PT AGA	38 (21.1%)	7 (17.1%)	18.4%

Table 2: Distribution of study subjects and incidence of hypoglycemia based on birth weight and gestational age

Characteristics		Number (%) N=180	Neonates with hypoglycemia (N=41) Number (%)	Incidence of hypoglycemia (%)
Gender	Male	118 (65.6%)	29 (70.7%)	24.6%
	Female	62 (34.4%)	12 (29.3%)	19.4%
Gravida	Primigravida	93 (51.7%)	29 (70.7%)	31.2%
	Multigravida	87 (48.3%)	12 (29.3%)	13.7%
Mode of Delivery	Vaginal delivery	109 (60.6%)	23 (56.1%)	21.1%
	LSCS	71 (39.4%)	18 (43.9%)	25.3%

DISCUSSION

In the present study, out of 180 LBW (≥ 1.8 < 2.5 kgs) babies, hypoglycemia was noted in 41 neonates with an incidence of 22.7%. Other studies conducted on hypoglycemia in low birth weight

neonates have noted an incidence varying from 22% to 32.5%⁷⁻¹²

Variations in incidence of hypoglycemia in different studies could be due to different cut offs of blood glucose levels used for defining hypoglycemia, variations in the population enrolled in the studies and also variations in the feeding practices of newborns. Out of 41 neonates with hypoglycemia, most of them (85.4%) were asymptomatic with only 14.6% being symptomatic. Other studies have also noted most of cases of hypoglycemia to be asymptomatic. Bhat Y R et al and Hotayana NA et al found 82.6% and 80% of the hypoglycemic neonates in their studies to be asymptomatic respectively.^{9,13} Most of the symptoms associated with hypoglycemia are non specific and include irritability, jitteriness, seizures, lethargy and poor feeding. Since most of the neonates are asymptomatic, screening for hypoglycemia is necessary in LBW neonates to detect hypoglycemia early and treat it before symptoms appear. Symptomatic hypoglycemia is known to have poor neurodevelopmental outcome.⁷

Most of neonates (70.7%) in the present study developed hypoglycemia in first 24 hours of life. Bhat Y R et al, Saini A et al and Natta VRS et al have also noted maximum incidence in first day of life.^{9,10,12} Therefore, ensuring adequate breast feeding soon after birth and monitoring of blood glucose levels more frequently in first day of life at 1,2,6,12 and 24 hours is necessary.

Most neonates (58.5%) in the study had only one episode of hypoglycemia. This finding has also been noted in studies by Singh P et al and Amarendra M et al, where most neonates had only one episode of hypoglycemia.^{11,14} Timely and proper management of the first episode with frequent breast feeds and if needed with formula feeds and IV dextrose can prevent further episodes. Cases of recurrent hypoglycemia should be investigated further and other causes like sepsis should be ruled out.

Incidence of hypoglycemia was higher in late preterms at 27.4% compared to 16.2% in term neonates. Studies by Acharya E et al, Bhat Y R et al, Saini A et al and Singh P et al have also noted a higher incidence in preterm neonates between 34-36 weeks gestation compared to those > 37 weeks.^{7,9,10,11} Late Preterm neonates are more prone to develop hypoglycemia because they are at risk of disordered neonatal metabolic adaptation. In the enterally fed infant, the source of circulating glucose is lactose from milk and between feeds from hepatic glycogenolysis and gluconeogenesis. If there is insufficient exogenous supply of glucose and the infant fails to switch on glycogenolysis or gluconeogenesis, hypoglycemia occurs. Immature hepatic enzyme system and impaired counter regulatory hormone response lead to hypoglycemia.

Neonates with birth weight ≥ 1.8 kg < 2.2 kg were slightly more prone to hypoglycemia than those ≥ 2.2 kg. Bhat Y R et al, Natta VRS et al, Amarendra M et al have also noted that lower the birth weight more is the risk for developing hypoglycemia.^{9,12,14} Reasons for hypoglycemia in LBW neonates include poor hepatic glycogen stores, poor feeding, lethargy and higher incidence of hypoxia and hypothermia.¹⁰

In the present study, the incidence of hypoglycemia in SGA babies was more than in AGA babies at 27.9% against 17.1%. Highest risk was noted in PT-SGA neonates. Increased risk in SGA neonates has also been noted in other studies.^{7,8,10,11} Shirley AS et al who studied hypoglycemia in SGA neonates noted that incidence of hypoglycemia was more in PT SGA neonates at 37.5% compared to FT-SGA at 17.65% and the findings were statistically significant ($P < 0.05$).¹⁵ SGA babies are at increased risk due to decreased glycogen stores and impaired gluconeogenesis. They have decreased alternate energy sources, deficient counterregulatory hormones and increased insulin resistance. They are more prone to hypoxia and hypothermia which worsen hypoglycemia.^{5,15} Therefore early enteral feeds in form of breast milk and if required supplementation with formula feeds or IV dextrose is necessary to prevent hypoglycemia especially in PT SGA babies.

The incidence of hypoglycemia in LBW male neonates was slightly more at 24.6% as against 19.4% in female neonates. Most studies have shown a slightly higher incidence of hypoglycemia in males compared to females but the difference has not been found to be statistically significant.^{10,12,16}

Neonates born to primigravida mothers had an increased risk of hypoglycemia compared to those born to multigravida mothers (31.1%

against 13.7%) Studies by Amarendra M et al, Shirley AS et al and Samayam P et al have shown an increased risk in neonates of primigravida mothers.^{14,15,17} They noted that primigravida mothers tend to face more difficulty related to breast feeding and so this group of neonates need to be monitored more closely for hypoglycemia.

In the present study, babies delivered by LSCS showed a slightly higher incidence of hypoglycemia compared to those delivered vaginally. Studies by Saini A et al and Burdan DR et al have also noted increased incidence in babies delivered by Cesarean section.^{10,18} Kayiram SM noted higher mean blood glucose levels in neonates delivered vaginally compared to those delivered by cesarean section.¹⁹ Infant delivered by LSCS may have less time for hormonal transition to occur compared to those delivered after normal labour. Also, delayed lactogenesis, delayed skin to skin contact and impaired thermoregulation may also contribute to hypoglycemia in these neonates.

CONCLUSION

Hypoglycemia is a common problem in low birth weight neonates, especially in preterm and SGA neonates. Prevention of hypoglycemia by early initiation of breastfeeding, early diagnosis of asymptomatic hypoglycemia by blood glucose monitoring and prompt treatment are necessary to minimize the severity and duration of hypoglycemic episodes which are associated with adverse neuro developmental outcomes.

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