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Original Research Article

Hypoglycemia in breastfed neonates: a hospital-based study

Abhishek Chakraborty[1]*, Monika Deb[2]

[1]Department of Pediatrics, [2]Department of Obstetrics and Gynecology, Jivan Jyoti Institute of Medical Sciences, Silchar Assam, India

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***Correspondence:**
Dr. Abhishek Chakraborty,
E-mail: abhismch12@gmail.com

ABSTRACT

Background: Neonates has well-coordinated adaptation system which maintains the blood sugar at certain safe level in extra uterine life. However certain intrauterine risk factors alter this adaptation system leading to hypoglycemia in early post-natal period. Most of the time hypoglycemic episodes are transient but sometimes there may be recurrent or prolonged hypoglycemia leading to permanent insult in brain and neurological deficit in post-natal life. Aims and objective of the study was to find out incidence of hypoglycemia in exclusively breastfeed neonates and the risk factors associated with this in the post-natal ward of a tertiary care centre in North-East India.
Methods: This is a prospective study conducted for a period of six month, where 112 exclusively breastfeed neonates who were shifted immediately to post-natal ward were included. Capillary blood sugar was checked at 1, 3, 6, 12, 24, 48 and 72 hours of life. Neonates with capillary blood glucose less than 40 were considered hypoglycemic. All the hypoglycemic babies were extensively evaluated for different intrauterine and post-natal risk factors.
Results: Incidence of hypoglycemia was 16% (18 out of 112 babies). Significant numbers (30.5%) of LBW babies had hypoglycemia, where as 6.5% of normal birth weight babies had hypoglycemia. 38.8% of preterm babies had hypoglycemia where as 11.95% of term babies had hypoglycemic episodes. 71.4% (5 out of 7 babies) of neonates born from diabetic mother. All the large for date infants of diabetic mother had hypoglycemia.
Conclusions: Our study came to a conclusion that incidence of hypoglycemia is not very uncommon finding in exclusively breastfeed neonates especially those with risk factors. Routine capillary blood glucose screening is utmost important to pick up the babies with hypoglycemia to prevent immediate and long-term complication.

Keywords: Hypoglycemia, Capillary blood glucose, Incidence, Neonates, Breastfeeeding

INTRODUCTION

Fetus in their intrauterine life receives glucose from maternal circulation via placenta through a facilitated diffusion. Enzymes necessary for gluconeogenesis remains very minimally active as there is very little need for glucose production.[1] At birth when the placental circulation is curtailed different metabolic adaptation occurs in neonate to fulfil the need of glucose supply. At birth glucose needs of neonates is approximately 5 to 8 mg/kg per minute mostly needed for cerebral use. Neonates gets the glucose from exogenous source (milk) and also by endogenous glucose production by glycogenolysis, gluconeogenesis and ketogenesis when adequate substrates are available.[1] The hormonal change that occurs at birth facilitate endogenous glucose production. Just after birth there is surge in glucagon and catecholamine production which helps to breakdown glycogen.[2] Within several hours of birth there is surge of growth hormone and cortisol which facilitates gluconeogenesis.[2] There is also decline in insulin secretion leading to fall in serum concentration of

insulin.[3] The initiation of milk feeding helps in gluconeogenesis and also helps in ketogenesis which spares glucose for cerebral use.[4] Defect in any adaptive pathway can cause hypoglycaemia in post-natal life and more likely when there is fasting.[2]

Hypoglycemia is a common metabolic disorder in neonates. Most of the time it is transient, mostly seen in preterm and small for date babies. It occurs due to developmental immaturity in gluconeogenesis and ketogenesis pathway and also due to depletion of glycogen stores due to stress and catecholamine secretion in intrauterine life.[5] The persistent forms of neonatal hypoglycemia may reflect inborn errors of metabolism , hypopituitarism with defects in the adrenocorticotropic hormone (ACTH)-cortisol axis together with deficiency of growth hormone, congenital defect in insulin secreation causing hyperinsulinism.[6] Hypoglycemia specially if persistent may cause seizure and permanent insult in brain leading to neurological deficit in post-natal life.[7,8] Proper glucose monitoring in post-natal life not only detects hypoglycaemia early but also prevents neurological complication in later life. Under this backdrop, this study was undertaken in a tertiary care hospital in North-East India to find out incidence of hypoglycaemia and the risk factor associated with it.

METHODS

The study was conducted in the post-natal word of Jivan Jyoti Institute of Medical Sciences, Silchar from 1st September 2022 to 28th February 2023. This was a prospective study. The study was conducted after getting ethical clearances from institutional ethical committee. A total of 112 newborn were included in this study. We included all the newborn who were immediately shifted with the mother following delivery (including both normal and LSCS) after obtaining consent from the parents. Newborn who required NICU admission at birth, step downed from NICU, Newborns with major congenital anomaly & neonates in whom other than breast milk was introduced were excluded from this study. Capillary blood glucose was estimated by heel prick method after confirming that heel was warm enough. Capillary Blood glucose was checked at 1, 3, 6, 12, 24, 48 and 72 hours of life. If any newborn was detected with hypoglycemia, then the baby was treated with standard protocol. Results were analyzed by statistical software (Number Cruncher Statistical Systems) NCSS 2023 and p value of less than 0.05 was considered statistically significant. Standard definitions were considered while classifying neonates in different groups. All the babies born before 37th completed weeks were considered as preterm while as babies born from 37th completed weeks to 42 completed weeks were considered as term neonates. Babies born after 42 completed weeks were considered as post term. Babies weighing less than 2.5kg were considered as low birth weight while babies weighing 2.5kg to 4kg were considered as normal birth weight. Babies weighing more than 4kg were considered as macrosomic. All babies weighing less than 10th centile for the gestational age were considered as SGA or small for gestational age, babies weighing 10th to 90th centile for the gestational age were considered as AGA or appropriate for gestational age while babies with birth weight more than 90th percentile were considered as LGA or large for gestational age babies.

Table 1: Demographic profile of enrolled cases.

Demographic profile		Number in each group (%)
Sex	Male	64 (52.4)
	Female	48 (47.6)
Gravida	Primi gravida	67 (59.8)
	Multi gravida	45 (40.2)
Maternal age (in years)	< 30	69 (61.6)
	>30	42 (38.4)
Mode of delivery	Vaginal Delivery	29 (25.8)
	LSCS	83 (74.2)

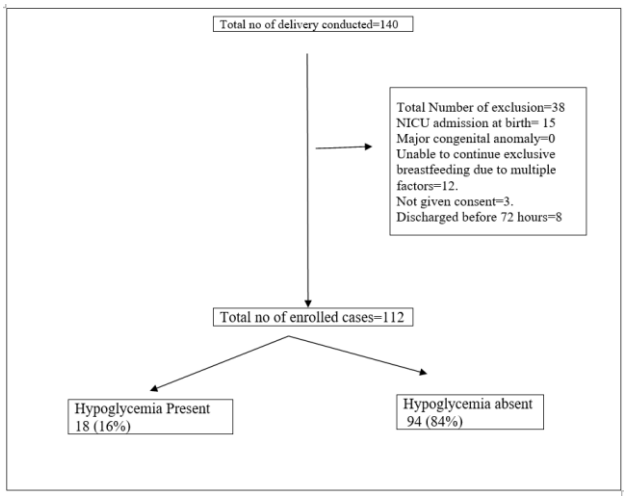

Figure 1: Flow diagram of the methodology in the present study.

RESULTS

A total of 140 deliveries were conducted in this 6-month period. Out of these 112 cases were enrolled in this study as per inclusion criteria. Demographics of these enrolled cases were shown in Table 1. Out of these 112 enrolled cases, 18 cases developed hypoglycemia in first 72 hours of life. Incidence of hypoglycemia in our study was 16%. Incidence of hypoglycemia was slightly more in male babies however this association was not found to be statistically significant.

In our study most of the cases with hypoglycemia were from primigravida mother. Hypoglycemia was more common in neonates born to mother younger than 30 years of age and however both these association were not

found to be statistically significant. We found incidence of hypoglycemia was more in babies delivered by LSCS (Table 2).

Table 2: Distribution of hypoglycemia in terms of sex and maternal factors.

Category	Total no (n)	Number of hypoglycemic neonates (%)	P value
Sex	Male (n=64)	10 (55.5)	0.88
	Female (n=48)	8 (44.5)	
Gravida	Primigravida (n=67)	12 (66.66)	0.51
	Multipara (n=45)	6 (33.33)	
Maternal age	<30 years (n=69)	14 (77.77)	0.12
	>30 years (n=42)	4 (22.23)	
Mode of delivery	Vaginal (n=29)	5 (27.78)	0.84
	LSCS (n=83)	13 (72.22)	

Table 3: Distribution of hypoglycemia in terms of neonatal factors.

Categories of neonates	Total cases	Hypoglycemia present (%)	P value
Term/AGA/ LBW-	13	3 (23)	0.09
Term / SGA/LBW	7	2 (28.5)	0.45
Term/AGA/IDM	3	2 (66.66)	1
Term/LGA	1	0 (0)	1
Term/LGA/IDM	2	2 (100)	0.5
Preterm/AGA with normal Birth weight.	5	0 (0)	0.06
Preterm /AGA/LBW	12	4 (33.33)	0.3
Preterm/SGA/LBW	4	2 (50)	1
Preterm/AGA/IDM	2	1 (50)	1
Term, AGA without any risk factor	61	2 (3.2)	0.01
Post Term /AGA	2	0	1

Out of 18 babies who developed hypoglycemia, 10 babies were male and 8 babies were female. In our study out of 112 enrolled cases 87 cases were term, 23 cases were preterm and 2 cases were post term. In our study 11 cases were small for gestational age (SGA), out of these 11 cases, 7 cases were Term SGA and 4 cases were Preterm SGA. In our study 36 babies were born with low birth weight. 3 cases were large for gestational age and all these cases were Term LGA. Out of these 3 LGA cases 2 were macrosomic both these babies were delivered from diabetic mother (IDM). We had two cases of preterm appropriate for gestational age babies born from diabetic mother.

In our study out of 13 cases of Term/AGA/LBW, 3 had developed hypoglycemia. Out of 7 cases of Term/SGA/ LBW, 2 babies developed hypoglycemia. In Preterm LBW babies, 12 were AGA. Out of these 12 babies 4 had hypoglycemia and 2 out of 4 cases of Preterm SGA babies had hypoglycemic episodes.

Table 4: Distribution of hypoglycemia according to birth weight.

Birth weight	Total cases	Hypoglycemia present (%)	P value
Low birth weight	36	11 (30.5)	0.02
Normal birth weight	74	5 (6.7)	0.01
Macrosomia	2	2 (100)	0.5

Out of total 36 LBW cases we had 11 cases of hypoglycemia. 5 babies out of 74 normal birth weight babies had hypoglycemia episodes in first 72 hours of life and both these association were found to be statistically significant (Table 4).

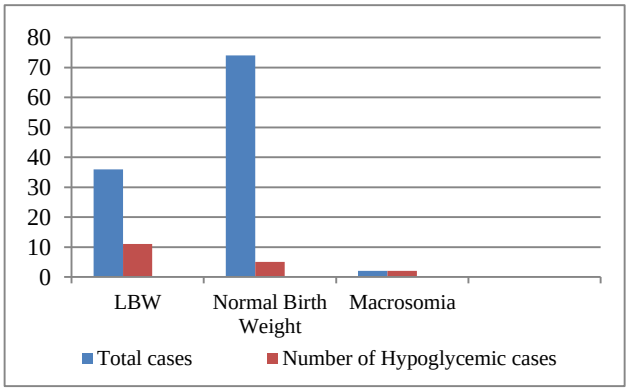

Figure 2: Distribution of hypoglycemia according to birth weight.

Table 5: Distribution of hypoglycemia according to gestational age.

Gestational age	Total cases	Hypoglycemia present (%)	P value
Pre term	18	7 (38.8)	0.4
Term	92	11 (11.95)	0.02
Post term	2	0 (0)	0.5

In our study there were 7 cases of infant of diabetic mother 5 cases were term whereas 2 cases were preterm. Out of 3 Term/AGA/IDM 2 had hypoglycemia. Both the two cases of Term/LGA/IDM cases had hypoglycemia. 50% (1 out of 2 cases) of preterm IDM cases had hypoglycemia.

Out of 61 term infants without any risk factor 2 cases developed hypoglycemia. Out of total 92 term babies 11 had hypoglycemia. These findings were statistically significant. Out of 2 post term cases none had hypoglycemia.

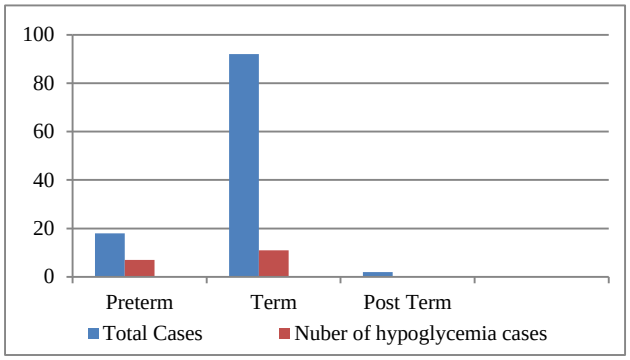

Figure 3: Distribution of hypoglycemia according to gestational age.

Out of 18 hypoglycemic neonates, 16 babies developed hypoglycemia in first 24 hours of life and rest 2 developed hypoglycemia beyond 24 hours of life, in fact both of them developed hypoglycemia within 48 hours of life.

DISCUSSION

In our study 16% (18 cases out of 112 enrolled cases) neonates admitted in post-natal ward had hypoglycemia in first 72 hours of life. Different studies worldwide had different incidence of hypoglycemia in exclusively breastfeed infants. Reason behind difference in incidence rates in different studies are multi-factorial. Different studies worldwide had different cut off level to diagnose hypoglycemia. Inclusion and exclusion criteria of various studies were also different. Other reasons behind different incidence rates are difference in race, ethnicity, access to healthcare facilities etc. Incidence rates of different studies worldwide were compared with our studies in Table 6.

Table 6: Comparison of incidence rates in different studies.

Studies	Year	Place	Incidence rates
Harries et al[9]	2012	Auckland, Newzealand	51%
Sashidharan et al[10]	2004	Kerela, India	42/1000 live births.
Singh et al[11]	2017	Meerut, India	67%
Turner et al[12]	2019	Boston, USA	40%
Zhou et al[13]	2015	Sanghai, China	16.9%
Present study	2022-2023	Silchar, Assam, India	16%

In our study incidence of hypoglycemia is slightly more in male babies (55.5%) in comparison to female babies (44.5%). However, this finding was not found to be statistically significant. Different studies done worldwide did not find any sex predilection for hypoglycemia in neonates.

In our study incidence of hypoglycemia were more in babies born from primigravida and also in babies born from mother's age less than 30 years of age. Though these association were not found to be statistically significant, the reason behind increase incidence of hypoglycemia in primi and young mother may be attributed to inexperience in breastfeeding practice. Study done by Kumar et al in Chennai, India also found higher incidence of hypoglycemia in neonates born to mother less than 30 years of age.[14] However in contrast to our study, Sashidharan et al and Turner et al, found more incidence of hypoglycaemia in neonates born to multiparity mother.[10,12] We found babies delivered by LSCS had more incidence of hypoglycaemia. Turner et al had similar findings.[12]

In our study, we found 30% of total LBW babies had hypoglycaemia episode in 1st 72 hours of life and it has statistically significant association. (Proportion test p value <0.05.) Similarly, we had 38.8% of total preterm neonates with hypoglycaemic episodes. In our study 28.5% of Term/SGA and 50% of preterm SGA babies had hypoglycaemia. Prematurity, LBW and small for gestational age are established risk factors for hypoglycaemia. Different studies done worldwide over the last few decades had proven this fact. Hyperinsulinism, increased calorie expenditure for thermoregulation are the reason behind hypoglycaemia in LBW and SGA babies. There is also relative excess of glucose-dependent tissues: high brain to liver ratio in SGA infants.

5 out of 7 IDM (71.4%) babies had hypoglycaemia and all of them had hypoglycaemia in 1st 2 hours of life indicating the importance of prompt & early sugar monitoring in infant born to diabetic mother. The rate of fall in blood glucose levels following delivery occurs earlier and is more pronounced among IDM.[15]

We found significant association of term and normal birth weight babies with hypoglycaemic episodes (proportion p value 0.02 and 0.01 respectively). However most of these cases had other associated risk factors like IDM, LGA/SGA babies etc. However, 3.2% of term babies without any associated risk factor had hypoglycaemia. However, most of those mothers were primipara and delivered by LSCS. Potential mechanisms that might mediate this association include delayed lactogenesis.

Limitations of our study is that study period was less and so number of cases enrolled were also. Another limitation of our study is that as per unit protocol we have taken a single cut off of less than 40 mg/dl to define

hypoglycaemia from birth to 72 hours of life, however literature shows that blood glucose level may go down upto 25mg/dl normally in 1st 4 hours of life and upto 35mg/dl in 1st 24 hours of life.[16] So cut-off less than 40mg/dl to diagnose as hypoglycaemia may lead to over diagnosis and over estimation of incidence of hypoglycaemia cases.

CONCLUSION

In this study we have seen that hypoglycaemia is quite common in post-natal ward specially in high-risk neonates, LSCS deliveries and in primi mothers with lack of confidence in breastfeeding. Capillary blood glucose monitoring in these cases may diagnose many asymptomatic hypoglycaemic neontates and proper management at appropriate time may prevent neonates to become symptomatic and prevent early and delayed neurological complication.

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