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Original Article

Paediatrics Section

Study of Asymptomatic Hypoglycemia in Full Term Exclusively Breastfed Neonates in First 48 Hours of Life

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ABSTRACT

Introduction: Hypoglycemia is a common metabolic problem in the neonatal period especially in the presence of settings like prematurity, small for gestational age babies and sepsis. Episodes of asymptomatic hypoglycemia may occur in term neonates without apparent risk factors.

Aim: This study was conducted to estimate the incidence of hypoglycemia in healthy, intramural, singleton full term neonates and to correlate the above incidence with maternal factors like parity, mode of delivery and time of initiation of breast feeding after birth.

Materials and Methods: A hospital based, prospective longitudinal study involving healthy, term, asymptomatic neonates. Blood glucose values were measured at 1, 6, 24 and 48 hours of life.

Results: The overall incidence of hypoglycemia was 10 % in asymptomatic, healthy term newborns. All the hypoglycemic episodes occurred in the first 24 hours of life. 23.07% of neonates born to primiparous mothers had hypoglycemia, against 5.4% neonates born to multiparous mothers ($p<0.05$). There was a higher recording of hypoglycemia when breast feeding was initiated > 1 hour after delivery (16.67%) than when breast feeding was initiated within one hour of delivery (7.89%).

Conclusion: Asymptomatic hypoglycemia occurred in about 10% of healthy, full term neonates; primiparity and delayed initiation of breast feeding > 1 hour are noted as additional risk factors.

Keywords: Healthy, Metabolic problem, Newborns, Term

INTRODUCTION

One of the commonest metabolic problems encountered in neonates is hypoglycemia. During intrauterine life there is a continuous supply of glucose to fetus from mother through placental transfer. When the umbilical cord is cut at birth, this supply of maternal glucose ceases abruptly. Hence, the neonate must maintain its own supply of glucose during periods of fasting and when feedings are interspersed intermittently [1]. During the transition from continuous transplacental supply of glucose to the intermittent oral supply postnatally, episodes of hypoglycemia can occur [2]. The developmental immaturity of adaptive mechanisms like gluconeogenesis, glycogenolysis and ketogenesis may further accentuate the occurence of hypoglycaemia [3]. The effects of hypoglycemia on the developing brain in neontaes and damage or sequelae caused in the long run are of great concern.

Healthy, full-term babies are functionally equipped to make the transition from their intrauterine into their extrauterine existence. There is no need for monitoring of these babies and interference with the natural breast feeding process is not advised. Term neonates have homeostatic mechanisms which help to preserve enough energy substrate to vital organs like brain [4]. The American Academy of Pediatrics and the World Health Organization recommend that blood glucose screening be done for at risk or symptomatic neonates. They conclude that universal hypoglycemia screening is not required, inappropriate and may also be potentially harmful [2]. However, there have always been concerns that hypoglycemia without clinical signs might also lead to neuro developmental sequelae [5,6]. Some studies have reported that long term neurological sequelae may be seen to the extent of 35% of newborns with symptomatic hypoglycemia and upto 20% in those with asymptomatic hypoglycemia [5,7]. There may be inadequate breast feeding due to various situations like primiparity, unfamiliarity with proper latching and breast feeding practices, post operative pain, sedation and discomfort in the mother that may interfere with the early, successful establishment of breast feeding even in healthy term neonates without any risk factors. We wanted to evaluate hypoglycemia occurring in these situations.

MATERIALS AND METHODS

This is a longitudinal study conducted over a nine months period in MVJ Medical College and Research Hospital, Hoskote, Bangalore, a rural tertiary care centre. Inclusion criteria: term, normal birth weight, healthy, CAN score 25 and above, asymptomatic singleton neonates delivered by vaginal route or LSCS in MVJ Medical College and Research Hospital. All babies were exclusively breast fed as per the BFHI (baby friendly hospital initiative) hospital policy and roomed in with their mothers, with good sucking reflex and latching and had an uneventful neonatal course. Informed consent was taken from the parents of babies included in the study. Ethical clearance was obtained from the Institutional ethical board. Babies were selected prospectively using a random number table. The following neonates were excluded from the study: small for gestational age, babies with evidence of fetal malnutrition (CAN score< 25), large for gestational age, preterm, neonates with birth asphyxia, sepsis (proven/suspected), neonates requiring admission in NICU / parenteral fluids/ other modes of feed, neonates born to mothers with PIH/ Diabetes.

For the study purpose hypoglycemia was defined as blood glucose <40mg/dl. Under aseptic precautions heel prick was made and capillary blood glucose was screened using reagent strips and Glucometer (one touch ultra easy meter) at 1,6,24 and 48 hours of life, independent of feeding time. Detailed history was taken; clinical examination and CAN score was done for all the neonates.

RESULTS

A total of 100 neonates were included in the study (males-48, females-52). Of this, 44 neonates were delivered by normal vaginal route and 56 were born through lower segment caesarean section. The clinical characteristics of the neonates included in the study are shown in [Table/Fig-1].

	Vaginal delivery (n=44) (SD±)	LSCS (n=56)(SD±)
Birth weight (grams)	2896.82(471.56)	2994.46(358.75)
Gestational age (weeks)	38.0 (0.68)	38.14 (0.84)
Males (n)	22	26
Females (n)	22	30
CAN score	28.39(0.895)	28.79(0.986)
Maternal age (years)	25.14(4.27)	23.5(2.52)
Primipara mothers	8	18
Multipara mothers	36	38

[Table/Fig-1]: The demographic and clinical characteristics of neonates in the study

The overall incidence of hypoglycemia was 10%. All these episodes of hypoglycemia were seen in the glucose values that were recorded at 1 hour and 6 hours of life. There were no episodes of hypoglycemia documented in the glucose values recorded at 24 and 48 hours of life.

There were 26 primiparous and 74 multiparous mothers in the study. Amongst the 26 primipara mothers, 6 neonates (23.07%) had hypoglycemia. Among neonates born to multiparous mothers, 4 had hypoglycemia (5.4%). The p value between these groups was significant (<.05). [Table/Fig-2] shows the charecteristics of babies born to primiparous vs mutiparous mothers and their glycemic distribution.

In this study, 44 neonates were delivered by vaginal route and 56 neonates were delivered by lower segment caesarean section. In the former group, 4 neonates had hypoglycemia, i.e. 9.1% of neonates delivered by vaginal delivery had hypoglycemia. In the latter group, 6 neonates had hypoglycemia, i.e. 10.7% of neonates delivered by LSCS. However the p-value between these groups was not significant (>0.05). [Table/Fig-3] shows the comparison of characteristics and glycemic distribution of babies born by vaginal route and LSCS.

Breast feeding was initiated at the earliest possible time after delivery in all the neonates. The neonates were divided into two groups based on the time of initiation of breast feeding. In 76 neonates breastfeeding was initiated within one hour life while in 24 neonates it was initiated more than one hour after birth. In neonates where breast feeding was initiated < 1 hour life, 6/76 episodes of hypoglycemia were documented (7.89%). In neonates where breast feeding was initiated > 1 hour of life, 4 episodes of hypoglycemia were documented (16.67%). The p value between these groups was 0.212 and not statistically significant.

DISCUSSION

Many studies have shown that early initiation of exclusive breast feeding meets the nutritional and metabolic needs of healthy, term neonates. Underfeeding alone does not cause symptomatic hypoglycemia in these neonates. Establishment of normal breast feeding may be interfered, when unnecessary supplementation of healthy term neonates with water, glucose water or formula is done [4,8,9]. According to present recommendations of the American Academy of Paediatrics and the World Health Organization, blood glucose screening should be reserved for at risk or symptomatic neonates. Healthy, term newborns experience normal, self-correcting physiologic blood glucose nadir around 1-3 hours of life. This physiologic nadir may be misidentified by early routine glucose screening in these neonates and aggressive treatment of this hypoglycaemia is unnecessary and inhibits the establishment of maternal-infant interactions [2].

In the present study, the nutritional status of all babies was assessed using simple Clinical Assessment of fetal Nutritional Status (CANS) and the CAN score was given. Evidence of loss of subcutaneous tissue and muscle was looked for; Examination of hair, cheeks, chin, neck, back, chest & abdomen, arms, buttock and legs was done and scored. Babies with CAN score 25 and above are considered normal. Those with score <25 are considered to have fetal malnutrition [9].

In the past, it has been estimated that 10% of normal term neonates are incapable to maintain a plasma glucose concentration above 30 mg/dl (1.7 mmol/L) when their first feed is delayed for about 3 to 6 hours post delivery [3,6]. Transient, asymptomatic hypoglycemia in healthy newborns may be a part of the normal transition to extrauterine life. However, persistent or recurrent hypoglycaemia may result in neurologic sequelae. Various threshold values for plasma glucose in the newborn infant have been described. Kalhan et al., summarised that in symptomatic neonates, plasma glucose concentrations of 45 mg/dl (2.5 mmol/l) or less should be considered as threshold for action. Asymptomatic babies and in those at risk for hypoglycemia, irrespective of gestational and postnatal age, threshold levels of plasma glucose values <36 mg/dl (2.0 mmol/l) should be considered [10].

		Age of mothers (years)	Birth weight (grams)	G1 (mg/dl)	G2 (mg/dl)	G3 (mg/dl)	G4 (mg/dl)	W1 (grams)	W2 (grams)	CAN score
Primi	Mean	21.84	2750	54.30	68.23	80.15	90.07	2625.38	2613.30	28.61
	± SD	2.072	380.026	12.04	11.26	25.93	21.98	398.28	397.96	1.09
Multi	Mean	25.054	3022.297	63.56	62.83	76.29	80.75	2918.91	2849.10	28.72
	± SD	3.50	402.702	15.66	16.12	20.05	19.14	367.60	376.28	0.925

[Table/Fig-2]: Glycemic distribution and population characteristics of babies born to Primiparous Vs Multiparous women (G1, G2, G3 and G4 - Glucose values at 1,6,24, and 48 hours of life
W1 and W2 are weight of neonates on day 1 and 2)

		Age of mothers (years)	Birth weight (grams)	G1 (mg/dl)	G2 (mg/dl)	G3 (mg/dl)	G4 (mg/dl)	W1 (grams)	W2 (grams)	CAN score
LSCS	Mean	23.50	2994.46	58.21	68.28	79.75	88.03	2884.28	2842.14	28.82
	± SD	2.52	358.75	12.06	13.37	23.93	21.13	335.26	321.86	0.93
NVD	Mean	25.13	2896.81	64.90	59.09	74.18	77.00	2789.54	2718.63	28.54
	± SD	4.27	471.55	18.09	15.83	18.14	17.34	459.66	464.84	0.99

[Table/Fig-3]: Glycemic distribution and population characteristics of babies born by LSCS Vs normal vaginal delivery (G1, G2, G3 and G4 - Glucose values at 1,6,24, and 48 hours of life
W1 and W2 are weight of neonates on day 1 and 2)

In our study on apparently healthy term neonates without any risk factors, we found an overall incidence of hypoglycemia of 10%. The blood glucose level that was used as a cut off was 40 mg/dl (2.2 mmol/l). De AK et al., found an incidence of hypoglycemia of 14.5% in term, normal birth weight newborns (blood glucose < 40 mg/dl) [11]. Lubchenco and Bard published in 1971, that appropriately grown full term infants had a 10% incidence of hypoglycemia when a serum glucose level < 30mg/dl was used [6]. Anderson et al., noted that 38% of term uncomplicated infants had blood glucose < 2.6mmol/l (47 mg/dl) in Kathmandu, Nepal [12]. [Table/Fig-4] shows these comparative studies in healthy asymptomatic term newborns.

Study	Blood glucose reference level	Incidence of hypoglycemia
Present study	< 40mg/dl	10%
De AK et al., [10]	< 40 mg/dl (2.2 mmol/L)	14.5%
Lubchenco and Bard [6]	< 30 mg/dl (1.7 mmol/L)	10%
Anderson et al., [13]	< 47mg/dl (2.6 mmol/L)	38%

[Table/Fig-4]: Comparative incidence of hypoglycemia with various blood glucose levels cut offs

A higher incidence of hypoglycemia was seen in neonates in delivered to primi mothers (23.07%) against neonates delivered to mutiparous mothers (5.41%) in our study with a significant p value between the two groups. Also, a higher incidence of hypoglycemia was found in the LSCS group (10.7%) than in the vaginal delivery group (9.1%). Sasidharan CK et al., concluded that hypoglycaemia was a common problem in apparently asymptomatic normal neonates. In addition to the classical risk factors, their study found that maternal oligohydramnios and a breastfeeding delay of greater than 2 hours after delivery also were risk factors for neonatal hypoglycaemia in this group [13]. In our study also we found that the incidence of hypoglycemia was higher in those neonates where breast feeding was initiated > 1hour after birth (16.67%), while it was lower (7.89%) in those neonates where breast feeding was initiated within one hour of life. The p value (> 0.05%) however was not significant. De AK et al., evaluated the role of early breastfeeding on hypoglycemia and also assessed the impact of exclusive breast feeding on glucose values up to 48 h of age in healthy normal birth weight and low birth weight babies, including both preterm and small for gestational age babies. They published that the incidence of hypoglycemia was significantly more in neonates when breast feeding was delayed than early breast feeding (64% vs. 17%; p<0.001) [11]. They also reported that healthy breastfed newborns had an overall incidence of hypoglycaemia of 32% and the blood glucose values increased as their hours of life increased. Maximum numbers of cases of hypoglycemia were seen within the first 24 hours of age. In our study also, we found that all the hypoglycemic episodes occurred in the first 24 hours of life. First time mothers and those who deliver by LSCS have many factors that may interfere with the early initiation of breast feeding and lactation like pain, discomfort, post operative sedation and delayed intake of full oral feeds. These may contribute to hindrance with early effective latching and breast feeding.

No considerable progress including evidence based studies have been undertaken to describe clinically important but transient neonatal hypoglycemia (as against persistent hypoglycemia from hyperinsulinemia), and how it relates to brain injury. New research to identify biomarkers that help to screen infants who may be at greater risk of neuro developmental injury and abnormal outcome due to low plasma glucose and other co morbidities needs to be undertaken [14]. The threshold for blood glucose level and the duration of hypoglycaemic episodes that may result in poor neuro developmental outcome in these healthy term neonates has not yet been established [15].

Moore et al., reported symptomatic hypoglycemia in otherwise healthy, breastfed term newborns. They reported three cases that presented at home on third day of life with seizures or life-threatening apnoeas. They postulated that early discharge of apparently normal neonates who have marginal metabolic or nutritional adaptation, may expose some neonates to post-discharge (still neonatal none the less) hypoglycemia and its attendant risks [16]. Buitendijk S et al., reported symptomatic hypoglycemia and seizures in two healthy breast fed term infants. They reported mild global developmental delay and cognitive impairment in these infants on follow up. They suggested that early recognition of risk factors such as hypothermia that lasts > 3 hours is essential to preventing hypoglycaemia. Also, in presence of risk factors, additional feeding may be warranted to maintain sufficient intake until breastfeeding can be adequately established [17].

LIMITATIONS

The limitation of the study is the small sample size. More studies with greater sample sizes are perhaps required to recognize the frequency and severity of hypoglycemia in asymptomatic healthy term neonates especially in the first 24 hours of life.

CONCLUSION

The study shows an incidence of hypoglycemia of 10% in first 24 hours of life in healthy, asymptomatic term neonates with normal CAN scores. This highlights that hypoglycaemia occurs in a significant number of these exclusively breast fed neonates which needs further systematic investigation. At present, the universal screening of uncomplicated term neonates for hypoglycemia is not recommended. This issue needs to be addressed as unrecognized hypoglycemia in these healthy neonates, in conjunction with hitherto unrecognized risk factors may result in long term neurological sequelae.

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