



INCIDENCE OF HYPOGLYCEMIA IN EXCLUSIVELY BREASTFED HIGH-RISK NEWBORNS

Pediatrics

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ABSTRACT

Background: Hypoglycemia is one of the commonest metabolic complications seen during neonatal period. In healthy newborns low blood glucose may not have much significance and merely reflect normal metabolic adaptation to extra-uterine life. However, in high-risk newborns, prolonged and/or recurrent episodes of hypoglycemia may negatively affect neurological and developmental prognosis. The incidence of hypoglycemia varies worldwide depending upon the blood sugar measurement protocols and feeding policies. There is paucity of data on incidence of hypoglycemia in institutions where exclusive breastfeeding is followed. **Aims and Objectives:** To determine the incidence and associated risk factors of hypoglycemia in first 72 hours of life among exclusively breastfed healthy high-risk newborns. **Study Design:** Observational study **Setting:** Department of Pediatrics, Nalanda Medical College and Hospital Patna, Bihar, India. **Period:** From 1st July 2019 to 31st December 2019. **Material & Methods:** The Observational study enrolled 560 exclusively breastfed high-risk newborns (infant of diabetic mother (IGDM/IDM), large-for-gestation (birth weight >90th percentile), small-for-gestation (birth weight <10th percentile), low birth weight (>1800 to <2500 grams) and late preterm), who did not require admission to neonatal intensive care unit and were kept in postnatal wards with mother. Babies on formula or pre-lactal feed, major congenital malformations and admitted in NICU for other reasons were excluded from the study. Hypoglycemia screening was done at 2, 6, 12, 24, 48 and 72 hours of life, prior to feeding. Hypoglycemia was defined as blood glucose ≤ 40 mg/dL (2.2 mmol/L). Blood glucose was estimated from heel prick capillary samples using glucometer. Association of both maternal and neonatal risk factors was studied in relation to hypoglycemia. **Result:** Incidence of hypoglycemia in high-risk newborns was 27.1%. Incidence was significantly higher in pre-term, low birth weight, Small-for-gestation age babies delivered to mothers with BMI >30 kg/m², born through caesarean section. **Conclusion:** in high-risk exclusively breast fed neonates blood glucose level should be regularly monitored for at least 1st 72 hours of life with special attention to 1st 24 hours.

KEYWORDS

Incidence, hypoglycemia, breastfed, small-for-gestation, low birth weight, late preterm

I. INTRODUCTION:

Neonatal hypoglycemia is one of the commonest metabolic problems encountered in neonatal medicine. In most of healthy neonates, these hypoglycaemic episodes are asymptomatic and do not adversely affect the short or long term outcome. They only reflect normal processes of metabolic adaptation to extrauterine life. However, when hypoglycaemic episodes are prolonged or recurrent, they may manifest with acute systemic effects and adverse neurologic outcome [1]. After 20 weeks of gestation, normal lower limit of concentration for fetal glucose is around 54 mg/dl [2], [3]. The fetus is completely dependent on mother for glucose, amino acids, free fatty acids, ketones, and glycerol supplies, to be used for its own energy needs. After birth, these newborns have to adapt from having a continuous source of glucose from the mother during intrauterine life to maintaining its own supply of glucose, both during periods of fasting and in between feedings [4]. Newborns' blood glucose concentration is about 70% of the maternal level, at the time of birth. It decreases further and reaches its nadir by about 1 hour of life to blood sugar level of around 20-25 mg/dl [5]. However, this nadir is transient and blood glucose level begins to rise again. The maintenance of normal glucose levels in newborns depends upon adequate glycogen stores, maturation of glycogenolytic and gluconeogenic pathways and an adequate integrated endocrine response. This postnatal adaptation is responsible for maintaining glucose homeostasis in a newborn [5-7]. Few newborns, especially in high risk group, including small for gestational age infants, preterm infants, and infants of diabetic mothers, fail to make this adaptation and are thus having altered glucose homeostasis and low plasma glucose levels [8].

The operational threshold for hypoglycemia is defined as "that concentration of plasma or whole blood glucose at which clinicians should consider intervention, based on the evidence currently available in literature". [8] This operational threshold for hypoglycaemia is currently believed to be a blood glucose value of <40mg/dl (plasma glucose <45mg/dl), in both term and preterm babies [9]. WHO defines hypoglycemia as blood glucose level of <45 mg/dl.

The risk factors for hypoglycemia are infants of diabetic mother (IDM), large for gestation age (LGA; birth weight >90th percentile), small for gestation age (SGA; birth weight <10th percentile), low birth weight and prematurity. Preventive measures, early recognition and prompt treatment of hypoglycemia are extremely important in these high risk neonates, to minimize any adverse outcomes associated with hypoglycaemic episodes [10].

Hypoglycemia could either be asymptomatic or symptomatic. When symptomatic, neonates might present with myriad of features like lethargy, irritability, jitteriness, apnoea, seizures etc. Adverse neuro-developmental outcomes have been documented with symptomatic hypoglycaemic episodes; however, outcomes of asymptomatic episodes are still uncertain. Both symptomatic and asymptomatic hypoglycaemic infants should be treated, as per unit protocol, to prevent any possible long term adverse effects [11, 12]

II. AIM AND OBJECTIVES:

This study was carried out to determine the incidence of hypoglycaemic episodes in exclusively breastfed, high-risk newborns, and to study the various associated high-risk factors like sex, gestational age, birth weight, maternal age, maternal BMI, Maternal morbidity like diabetes mellitus, hypertension, mode of delivery, parity and time of onset of the development of hypoglycemia etc.

III. MATERIALS AND METHODS

This observational, longitudinal, hospital-based study was carried out in the Department of Paediatrics (Postnatal ward and NICU) of Nalanda Medical College and Hospital (NMCH), Patna, Bihar, India from 1st July 2019 to 31st December 2019

Inclusion criteria:

Neonates given exclusive breast feed within half an hour after normal delivery and within one hour after a caesarean delivery, with any one of the following high-risk factors;

- 1) Small-for-gestational-age (SGA) infants: birth weight <10 percentile
- 2) Large-for-gestational-age (LGA) infants: birth weight >90 percentile
- 3) Birth weight <2500 grams (but >1800 grams)
- 4) Macrosomic infants: birth weight >4000 grams
- 5) Infant of diabetic mother (IDM): maternal type 1 or type 2 diabetes mellitus or gestational diabetes mellitus
- 6) Infants of hypertensive mother
- 7) Late preterm infant (LPI): a premature infant born between 34-36_{6/7} gestational weeks

Exclusion criteria:

any of the following;

- 1) Healthy term infants
- 2) Birth weight ≤ 1800 grams
- 3) Babies with congenital malformations
- 4) Newborns suffering perinatal asphyxia
- 5) Babies who are not able to be exclusively breast-fed in the first hour, due to any reason.
- 6) Infants with sepsis
- 7) Infants with polycythemia
- 8) Newborns in whom breastfeeding could not be initiated, continued or contraindicated, who required I.V. fluid and those given pre-lacteal or formula feeds
- 9) Newborns admitted to NICU due to other reasons
- 10) Multiple gestation babies
- 11) Babies whose parents have not given the consent
- 12) Babies who were discharged before 72 hours of birth

All neonates were weighed at birth with an electronic weighing machine with an accuracy of ±5gm. The birth weight percentiles were adopted from the Fenton growth charts. Gestational age assessment was done by the Modified New Ballard Score.

During the study period of six months duration, 790 babies born with risk factors for hypoglycemia were screened. Out of these, 560 met the inclusion criteria and were enrolled in the study. Parents of these were explained about baby's risk for hypoglycemia and consent for blood tests at regular intervals was obtained.

The detailed history of the enrolled babies was taken and relevant clinical examination was done. All the details of the newborn and mother were noted in a proforma at the time of enrolment. Infant's treatment plans were made according to the unit protocol. It was planned that these babies would be breastfed as soon as possible following birth, preferably within half an hour after normal delivery and within one hour after a caesarean delivery. Counselling as well as assistance for exclusive breastfeeding was done in all cases. Breastfeeding was ensured by either direct breast feeding or with expressed breast milk depending on gestational maturity and feeding skills within 30 minutes of birth in vaginal delivery and no later than one hour after caesarean section and thereafter every 2 to 3 hrs, including at least two-night time feeds.

Definition and classification of hypoglycemia

- 1) Hypoglycemia: blood glucose <40 mg/dL
- 2) Severe Hypoglycemia: blood glucose <25 mg/dL
- 3) Prolonged hypoglycemia: the baby is still hypoglycaemic after 1 h of intervention
- 4) Recurrent hypoglycemia: ≥2 hypoglycaemic episode

Blood glucose testing

Samples were collected by heel prick (capillary blood), under aseptic precautions. The blood glucose was measured using Accucheck active glucometer, which was calibrated monthly. Capillary blood samples were taken after warming the heels of the babies. Blood glucose levels were monitored at 2 hr of life and later at 6, 12, 24, 48 and 72 hrs of life or any time if symptomatic, preferably pre-prandial. Confirmation of blood glucose was done by obtaining the sample to the laboratory only if the capillary glucose level was less than 25 mg/dL, if three consecutive readings of BGL remained ≤40mg/dL or if the baby was symptomatic. The babies were observed for signs and symptoms attributable to hypoglycemia. Neonates detected to have hypoglycemia during this study were transferred to Neonatal Intensive Care Unit (NICU) and managed according to the standard institutional protocol.

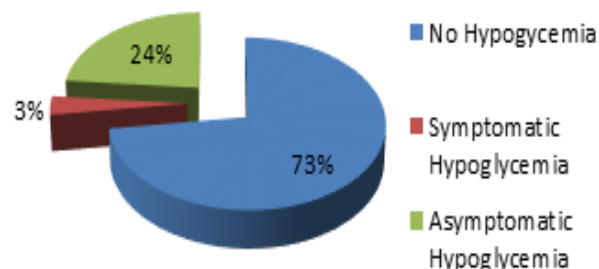
Statistical analysis

SPSS version 22.0 for Microsoft windows was used to analyze the data. Descriptive statistics were presented as number of observations and percentage (%). The clinical and laboratory parameters of the study population were expressed in terms of mean and ± standard deviation (SD). Nonparametric categorical data were compared with Chi-square test and parametric continuous data were compared with Student's t test. P values less than 0.05 were considered statistically significant. The relationship of hypoglycemia against age of onset, symptomatology, gestational age, birth weight and sex of the baby, parity and age of mother, and mode of delivery etc. were analysed.

IV. OBSERVATION & RESULTS

Total of 560 healthy newborns with risk factors were enrolled in this study, out of which 27.1% (n=152) developed at-least one episode of hypoglycemia within first 72 hours of life. Out of total 152 newborns developing hypoglycemia, 86.8% (n=132) had asymptomatic hypoglycemia, whereas 13.2 % (n=20) developed symptomatic hypoglycemia. (Figure 1).

Fig 1: Distribution of total patients



Among these 152 hypoglycaemic newborns, 60.5% (n=92) were male vs 39.5% (n=60) female, 80.9% (n=123) with preterm gestational age, 63.1% (n=96) with birth weight less than 2500 grams. Prematurity, birth weight <2.5kg and small for gestation age (SGA) were found to be independent significant risk factors for developing hypoglycemia.

Babies born to mothers with BMI >30 kg/m² had significantly higher (p<0.00001) incidences of hypoglycemia. Maternal age or morbidities like DM, HTN were not found to be significant independent risk factors. Babies born through lower segment Caesarean section (LSCS) had significantly higher chances of developing hypoglycemia (p=0.000096). Parity, antenatal booked or unbooked pregnancy and urban or rural residence were not found to be independent significant risk factors (Table 1).

Table 1: Clinical characteristics and incidence of hypoglycemia in high risk neonates.

Characteristics		Number (%) (total n=560)	Incidence of Hypocemia (%)	% Of total (n=152) Hypoglycaemic Patient	P-value	Asymptomatic hypoglycemia [n=132, 86.8%] (% of total hypoglycemia)	Symptomatic hypoglycemia [n=20, 13.2%] (% of total hypoglycemia)
Sex	Male	314 (56.1%)	92 (29.3%)	60.5%	0.2137	75 (49.3%)	17 (11.2%)
	Female	246 (43.9%)	60 (24.4%)	39.5%		57 (37.5%)	03 (2.0%)
Gestation Age	Preterm	398 (71.1%)	123 (30.9%)	80.9%	0.0066	111 (73%)	12 (7.9%)
	Term	147 (26.2%)	27 (18.3%)	17.7%		20 (13.1%)	7 (4.6%)
	Post Term	15 (2.7%)	2 (13.3%)	1.3%		1 (0.6%)	1 (0.6%)
Birth Weight	<2500 gm	292 (52.1%)	96 (32.8%)	63.1%	0.0057	83 (54.6%)	13 (8.5%)
	2500-3999 gm	198 (35.3%)	40 (20.2%)	26.3%		34 (22.3%)	6 (3.9%)
	>4000 gm	70 (12.5%)	16 (22.8%)	10.5%		15 (9.8%)	1 (0.6%)

Status at birth	LGA	84 (15%)	16 (19.0%)	10.5%	0.0029	15(9.8%)	1(0.6%)
	AGA	348 (62.1%)	87 (25.0%)	57.2%		73 (48%)	14 (9.2%)
	SGA	128 (22.8%)	49 (38.2%)	32.2%		44 (28.9%)	5 (3.3%)
Maternal Age	< 30 years	124 (22.1%)	36 (29.0%)	23.6%	0.6472	28 (18.4%)	8 (5.2%)
	>30 years	436 (77.8%)	116 (26.6%)	76.3%		104 (68.4%)	12 (7.9%)
Maternal BMI (kg/m ²)	18.5-25	242 (43.2%)	16 (6.6%)	10.5%	<0.00001	10 (6.5%)	6 (3.9%)
	25-30	212 (37.8%)	62 (29.2%)	40.7%		54 (35.5%)	8(5.2%)
	>30	106 (18.9%)	74 (69.8%)	48.6%		68 (44.7%)	6(3.9%)
Maternal Morbidity	DM	196 (35%)	56 (28.5%)	36.8%	0.8127	48 (31.6%)	8(5.2%)
	HTN	180 (32.1%)	50 (27.7%)	32.9%		44 (28.9%)	6(3.9%)
	DM +HTN	58 (10.3%)	16 (27.5%)	10.5%		14 (9.2%)	2 (1.3%)
	None	126 (22.5%)	30 (23.8%)	19.7%		26 (17.1%)	4 (2.6%)
Mode of Delivery	NVD	225 (40.1%)	40 (17.7%)	26.3%	0.000096	36 (23.6%)	4 (2.6%)
	LSCS	319 (56.9%)	109 (34.1%)	71.7%		94 (61.8%)	15 (9.8%)
	Assisted	16 (2.8%)	3 (18.75%)	1.9%		2 (1.3%)	1 (0.6%)
Parity	Primigravida	325 (58%)	88 (27.0%)	57.9%	1.0000	76(50%)	12 (7.9%)
	Multigravida	235 (42%)	64 (27.2%)	42.1%		56 (36.8%)	8 (5.2%)
Antenatal History	Booked	202 (36%)	48 (23.7%)	31.6%	0.1986	42 (27.6%)	6(3.9%)
	Unbooked	358 (64%)	104 (29.0%)	68.4%		90 (59.2%)	14 (9.2%)
Residence	Urban	246 (44%)	67(27.2%)	44.1%	1.0000	59(38.8%)	8 (5.2%)
	Rural	314 (56%)	85 (27.07%)	55.9%		73 (48%)	12 (7.9%)

Amongst newborns who developed at least 1 hypoglycemia episode, 85.5% (n=130) did so within 24 hours of life (Table 2). Hypoglycemia was observed more frequently in first 2 hours as compared to next 70 hours.

Table 2: Incidence of hypoglycemia in relation to days of life

Days of life	1 st	2 nd	3 rd
Cases of hypoglycemia (n=152)	130 (85.5%)	16 (10.5%)	6 (3.9%)

Out of 152 hypoglycaemic neonates, 84 (55.2%) had only one episode of hypoglycemia, 42 (27.6%), 13 (8.5%) and 7 (4.6%) newborns had 2, 3 or more than 3 episodes of hypoglycemia respectively (Table 3).

Table 3: No. of episodes of Hypoglycemia

No of episodes of hypoglycemia	No. of cases (%)	% of total (n=560)
1 episode	84 (55.2%)	15%
2 episodes	42 (27.6%)	7.5%
3 episodes	13 (8.5%)	2.3%
>3 episodes	7 (4.6%)	1.25%
Total	152	27.1%

V. DISCUSSION:

In the present study, out of 560 newborns, 152 newborns were found to be hypoglycaemic whereas 408 newborns did not have hypoglycemia. Hence the incidence of hypoglycemia in exclusively breastfed but high-risk neonates was 27.1% (Fig 1). Singh et al in an Indian study have reported 27% incidence of hypoglycemia in high risk infants [13]. 27.1% incidence in our study is also comparable to incidence of 24% in study done by Amarendra M et al [14], 20% by Patel P et al [15] and 33.3% found by Kumar TJ et al [16]. There were no episodes of severe hypoglycemia in our study and only 13.2% of hypoglycaemic babies were symptomatic.

In our study, the incidence of hypoglycemia in male neonates was found to be more than female neonates (29.3% vs. 24.4%). However, when the incidence of hypoglycemia was compared with each other it was concluded that hypoglycemia in exclusively breastfed high-risk newborns, did not have any sex predilection ($p=0.2137$). This observation was similar to the studies conducted by Singh et al [13], Patel p et al [15], Saini A, et al. [17], and a study conducted by Stark J, et al [18].

The incidence of hypoglycemia was significantly higher in preterm babies at 30.9% ($p=0.0066$), which is similar to incidence of 36.9% found in study done by than Singh et al [13]. The incidence of hypoglycemia shown by various other previous studies in preterm infants were 4.3% by Chance & Brower,[19], 3-15% by Hawdon,[20] 12.8% by Singhal et al.[21] 15% by Fluge,[22]. The incidences of hypoglycemia in preterm babies were significantly higher at 67% in study by Lubchenco and Bard [23] and at 77.7% in De et al study [24]. Reason for wide variation in incidences of hypoglycemia among various studies could be due to different cut-off defined for hypoglycemia and the fact that in some studies preterm babies are with

morbidity like very low birth weight (<1500 grams), RDS etc., were admitted in NICU admission and hence were excluded from the study.

The incidence of hypoglycemia in low birth weight newborns was 32.8%, which was significantly higher ($p=0.0057$). Singh et al study showed incidence of hypoglycemia in low birth weight newborns 29.5%, Saini et al showed 24%, De et al showed 64.8% incidence of hypoglycemia in low birth weight newborns [13, 17, 24].

The incidence of hypoglycemia was 38.2% in SGA, which is higher than that with the Holtrop et al and in Bhat et al reports [25, 26]. In Holtrop et al the frequency of hypoglycemia in SGA infants was 14.7% [25]. In Bhat et al study, the incidence of hypoglycemia was 25.2% in SGA babies [26]. De et al study showed incidence of hypoglycemia in SGA was 64.2%, but the population size was very small [24]. Holtrop, et al had excluded newborns of diabetic mothers and their newborns were not exclusively breastfed [25]. Bhat, et al included all SGA newborns, whether breastfed, formula-fed, or on intravenous fluids. These factors could have lowered the incidence of hypoglycemia in their studies [26]. High incidence of hypoglycemia in SGA in our study can be explained due to high risk pregnancies managed in our institution. The frequency of hypoglycemia in LGA infants was 5% in Holtrop et al study and 14.6 % in Singh et al study [25, 13]. The incidence of hypoglycemia in LGA in this study was 19%.

We found that the incidence of hypoglycemia in newborns was higher (29%) when maternal age was < 30 years, which was similar to findings in study by Kumar TJ, et al. [27] in the year 2018, where they found that the incidence of hypoglycemia in infants born to mothers less than 30 years of age was 38%, while the incidence in infants born to ≥ 30 years was 18.9%.

The incidence of hypoglycemia was found to be 28.5% in Infant of diabetic mothers. The incidence of hypoglycemia in IDM was found to be 28.6% in Singh et al study and 30% in Cordero et al study [13, 28]. In the present study, the incidence of hypoglycemia in babies born to mothers with hypertension was 27.7% whereas the incidence in babies born to hypertensive mothers reported by Singh et al. was 33.3% [13].

Incidence of hypoglycemia was higher in newborns delivered through LSCS in comparison to those born through NVD (34.1% vs 17.7%; $p<0.05$). It is in contrast to study done by K K Divakar et al [29] and Hawdon et al [30] on neonates, where they found that the mode of delivery does not affect the blood glucose of the baby. This difference in observation could be due to different inclusion and exclusion criteria among these studies and/or might be due to higher numbers of LSCS performed at our institute due various fetal and maternal reasons.

In our study, there was no difference in incidence of hypoglycemia in newborns delivered to either primigravida or multigravida mothers. In a study by Sasidharan CK, et al. [31] the neonates of multigravida mothers had a higher incidence of hypoglycemia than primigravidae. But result was different in the study which was conducted by Purnima Samayam, et al. [32] in the year 2015 where they found 23.07% of

neonates born to primiparous mothers had hypoglycemia, against 5.4% neonates born to multiparous mothers.

The incidence of hypoglycemia was highest (85.5%) on the first day of life. Furthermore most of day 1 episodes occurred within first 2 hours of life. According to Hawdon et al in a study on preterm infants the mean blood glucose concentration was significantly lower on the first day than on subsequent days [30]. Likewise, in a study by MA Bhat et al on SGA babies, almost all the episodes of hypoglycemia occurred within 24 hours [26]. In our study hypoglycemia was seen upto 3rd day of life suggesting the need for constant monitoring of blood glucose values in the first 72 hours with special attention within 1st 2 hours of life.

The wide variation in the incidences of hypoglycemia among various high-risk category newborns across different studies could be attributable to the differences in definitions of hypoglycemia, the method and frequency of blood glucose monitoring, feeding methods and frequency. Furthermore there was vast difference in inclusion and exclusion criteria among different studies. Demographic profile, birth weight and gestational age of the neonates also varied among different studies. Population characteristics may also have led to variation in the figures of incidence. There is no universally accepted Point-Of-Care (POC) method to identify the low level of blood glucose accurately and reliable to use it as the sole method of screening for hypoglycemia in newborn at risks. There also is marked variability in obtaining and processing blood samples for analyses of glucose concentrations and the incidence also varies according to it. Symptomatic hypoglycemia should be treated with parenteral glucose infusion. Breastfeeding is the initial management of asymptomatic hypoglycemia. Different units follow different protocols for management of asymptomatic hypoglycemia. The incidence of hypoglycemia varies according to the protocols and feeding methods. There is a paucity of data on the incidence of hypoglycemia where exclusive breastfeeding policy is followed.

Even in the presence of an arbitrary low glucose level, the physician must assess the general status of the infant by observation and physical examination to rule out other disease entities and processes that may need additional laboratory evaluation and treatment

VI. CONCLUSION:

The present study has shown that significant percentage of high-risk babies who are on exclusive breast feed developed hypoglycaemia. We conclude that healthy high-risk newborns in the postnatal ward can be exclusively breastfed, but their blood glucose levels need to be monitored at least for the first 72 hours with the greatest emphasis on the first 24 hrs and asymptomatic hypoglycemia in newborns need to be detected and managed promptly. Newborns with risk factors for hypoglycemia should be screened at regular interval for blood glucose level more specifically at first 24 hours of life in order to prevent hypoglycemia and potential neuro-developmental damage.

VII. LIMITATIONS:

This was a single centric study with moderate sample size. There's need for larger multi-centric study for any generalized recommendations to be made.

VIII. CONFLICT OF INTEREST:

None

IX. FINANCIAL DISCLOSURE:

The authors declare that this study has not received any financial grant.

REFERENCES:

- 1) Cornblath M, Hawdon JM, Williams AF, Aynsley-green A, Ward-platt MP, et al. (2000) Controversies regarding definition of neonatal hypoglycemia : Suggested operational thresholds. *Pediatrics* 105: 1141-1145.
- 2) Kahler SG. Metabolic disorders associated with neonatal hypoglycemia. *Neo Rev*. 2004;5.
- 3) Kalhan SC, D'Angelo L, Savin SM, Adam PAJ. Glucose production in pregnant women at term gestation: Sources of glucose for human fetus. *J Clin Invest*. 1979; 63:388-94.
- 4) Murty VY, Ram KD (2012) Study of pattern of blood sugar levels in low birth weight babies who are exclusively on breast milk. *J Dr NTR Univ Heal Sci* 1: 90-93.
- 5) Srinivasan G, Pildes RS, Cattamanchi G, Voora S, Lilien LD. Plasma glucose values in normal neonates: a new look. *J Pediatr*. 1986;109:114-7.
- 6) Heck LJ, Erenberg A. Serum glucose levels in term neonates during the first 48 h of life. *J Pediatr*. 1987;110:119e22.
- 7) Adamkin DH. Update on neonatal hypoglycemia. *Archs Perinat Med*. 2005;11:13e5.
- 8) Harris DL, Weston PJ, Harding JE (2012) Incidence of neonatal hypoglycemia in babies identified as at risk. *J Pediatr* 161: 787-791.
- 9) Cornblath M. et al. Controversies regarding definition of neonatal hypoglycemia:

- suggested operational thresholds. *Pediatrics*. 2000;105:1141-5
- 10) Kaiser JR, Bai S, Gibson N, Holland G, Lin TM, et al. (2015) Association between transient newborn hypoglycemia and fourth-grade achievement test proficiency: A population-based study. *JAMA Pediatr* 169: 913-921.
- 11) Lucas A, Morley R. Outcome of neonatal hypoglycemia. *Br Med J*. 1999;318:194.
- 12) Filan PM, Inder TE, Cameron FJ. Neonatal hypoglycemia and occipital cerebral injury. *J Pediatr*. 2006;148:552-5.
- 13) Singh, P., Upadhyay, A., Sreenivas, V. et al. Screening for hypoglycemia in exclusively breastfed high-risk neonates. *Indian Pediatr* 54, 477–480 (2017). <https://doi.org/10.1007/s13312-017-1051-0>
- 14) Amarendra M et al. *Int J Contemp Pediatr*. 2018 May;5(3):944-948
- 15) Patel P, Gogoi PR, Deb S, Paul P, Yesmin S, et al. (2020) Hypoglycemia in Exclusively Breastfed High-Risk Neonates - A Hospital-Based Study. *Int J Pediatr Res* 6:066. doi.org/10.23937/2469-5769/1510066
- 16) Kumar TJ et al. *Int J Contemp Pediatr*. 2018 Sep;5(5):1952-1955
- 17) Saini A, Gaur BK, Singh P (2018) Hypoglycemia in low birth weight neonates: Frequency, pattern, and likely determinants. *IJCP* 5: 526-532.
- 18) Stark J, Simma B, Blassnig-ezeh A (2019) Incidence of hypoglycemia in newborn infants identified as at risk. *J Matern Neonatal Med*, 1-6.
- 19) G. W. Chance, B. D. Bower. Hypoglycemia and Temporary Hyperglycemia in Infants of Low Birth Weight for Maturity. *Arch Dis Child*. 1966; 41: 279-285
- 20) J. M. Hawdon. et al. "Patterns of metabolic adaptation for preterm and term infants in the first neonatal week". *Archives of Disease in Childhood*. 1992; 67: 357-365.
- 21) Singhal P.K et al. "Neonatal hypoglycemia-clinical profile and glucose requirements". *Ind. Pediatr*. 1999; 134:492-498.
- 22) Fluge G. Clinical aspects of neonatal hypoglycemia. *Acta Paediatrica Scandinavica*. 1974; 63: 826-832.
- 23) Lubchenco L.O, Bard H. Incidence of hypoglycemia in newborn infants classified by birth weight and gestational age. *Pediatrics*. 1971; 47: 831-838.
- 24) De AK, Biswas R, Samanta M, Kundu CK. Study of blood glucose level in normal and low birth weight newborns and impact of early breast-feeding in a tertiary care Centre. *Ann Nigerian Med*. 2011;5:53-8.
- 25) Holtrop PC. The frequency of hypoglycemia in full term large and small for gestational age newborns. *Am J Perinatol*. 1993;10:150-64.
- 26) Bhat MA, Kumar P, Bhansali A, Majumdar S, Narang A. Hypoglycemia in small for gestational age babies. *Indian J Pediatr*. 2000;67:4.
- 27) Kumar TJ, Vaideeswaran M. AST (2018) Incidence of hypoglycemia in newborns with risk factors. *Int J Contemp Pediatr* 5: 1952-1955.
- 28) Cordero L, Thung S, Landon MB, Nankervis CA. Breast-feeding initiation in women with pregestational diabetes mellitus. *Clinical Pediatr*. 2014;53(1):18-25.
- 29) K K Diwakar, M V Sasidhar. "Plasma glucose levels in term infants who are appropriate size for gestation and exclusively breast fed" *Arch Dis Child Fetal Neonatal Ed*. 2002;87:46-48.
- 30) J. M. Hawdon. et al. "Patterns of metabolic adaptation for preterm and term infants in the first neonatal week". *Archives of Disease in Childhood*. 1992; 67: 357-365.
- 31) Sasidharan CK, Gokul E, Sabitha S (2004) Incidence and risk factors for neonatal hypoglycaemia in Kerala, India. *Ceylon Med J* 49: 110-113.
- 32) Samayam P, Balasundaram R (2015) Study of asymptomatic hypoglycemia in full term exclusively breastfed neonates in first 48 hours of life. *J Clin Diagnostic Res* 9: 7-10.