Original Article

Incidence of Hypoglycaemia and its Determinants in Neonates Admitted in Neonatal Intensive Care Unit

Indumathi Manoharan[1] , **Vetriselvi Prabakaran[2]*** , **Adhisivam Bethou[3]**

[1]College of Nursing, Jawaharlal Institute of Post Graduate Medical Education and Research (JIPMER), Puducherry, India
[2]Department of Pediatric Nursing, College of Nursing, Jawaharlal Institute of Post Graduate Medical Education and Research (JIPMER), Puducherry, India
[3]Department of Neonatology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) Puducherry, India

Abstract

Introduction: Baby in mother's womb depends on placental circulation for glucose. During birth, the clamping of the umbilical cord abruptly curtails the glucose supply from the placenta and thus neonates are more prone to develop hypoglycaemia and is preventable if we aware of the maternal and neonatal risk factors. This study aimed to identify the incidence of hypoglycaemia and its risk factors.

Methods: A prospective observational design was carried out among 115 neonates in neonatal intensive care unit (NICU) during December 2021 to January 2022. Convenience sampling technique was used to enrol the neonates who met the inclusion criteria. Neonatal and maternal clinical characteristics, incidence, risk factors of hypoglycaemia, were collected by direct observation and from medical record. Data were analysed using chi-square test, *t* test and logistic regression with SPSS software version 25.

Results: The incidence of hypoglycaemia was 30.4% .20.8 % had single episode and 9.6% had multiple episodes. Mean (SD) lowest blood glucose value was 11.31 (17.91). Mean (SD) age at which first episode detected was 6.33 (16.05) hours. Predominant symptoms were jitteriness, lethargy and convulsion. Hypothermia, sepsis, prematurity, small for gestation, intra uterine growth retardation, birth asphyxia, history of poor feeding, birth weight, twin pregnancy, gestational diabetes mellitus were associated with neonatal hypoglycaemia significantly.

Conclusion: Incidence of neonatal hypoglycaemia can be minimized by identifying the risk factors, adhering close monitoring and by early treatment. This will prevent poor neurodevelopmental outcomes.

Introduction

Hypoglycaemia is one of the metabolic problems occurs in the neonatal period.[1] Glucose is the sole energy source for brain development during neonatal period.[2] Neonates have high energy requirements and insufficiency of the enzyme and substrates involved in energy production in this period can lead to hypoglycaemia.[3] The incidence of hypoglycaemia in newborns is estimated to be 1-3 per 1000 live births.[4] The foetus depends on maternal metabolism and placental circulation to provide glucose, free fatty acids and amino acids which are necessary to meet its energy requirements and during birth abrupt cessation of glucose supply from the placenta leads to hypoglycemia.[5] Undiagnosed hypoglycaemia can have long term neurological consequences.[6] Usually the transition from intra-uterine glucose regulation to extra-uterine adaptation develops in first 24 hours of age.[7] The most common metabolic abnormality in newborns is hypoglycaemia and this results in increased morbidity and mortality.[8] Severe glucose deficiency can potentially leads to cerebral energy failure and impaired cardiac performance.[9] Hypoglycaemia which lasts for prolonged period or recurrent hypoglycaemic episodes may result in poor neurological development in neonates.[10] Untreated hypoglycaemia may leads to mental retardation of varied severity.[11] The prognosis of new born who had hypoglycaemia depends on how promptly and efficiently it is managed.[12,13]

In-spite of advancing health care system the admission of neonates to the neonatal unit with hypoglycaemia had been increasing. Thus identifying the risk factors of neonatal hypoglycaemia is very essential to formulate the prevention policy in neonatal unit. Even though some risk factors were documented in literature, these factors are centre specific. Hence we can expect the difference in strength of association between the risk factors and the

incidence of hypoglycaemia.

Only few studies have been conducted to identify the incidence of hypoglycaemia among neonates. A study conducted among 50 neonates in a neonatal unit and reported that 30% had hypoglycaemia.[14] De et al reported that among 150 neonates 32% had hypoglycemia.[15] Practice Essentials Neonatal hypoglycaemia is defined as a plasma glucose level of less than 30 mg/dL (1.65 mmol/L) in the first 24 hours of life and less than 45 mg/dL (2.5 mmol/L) thereafter is the most common metabolic problem in newborns. Major long-term sequelae include neurologic damage resulting in mental retardation, recurrent seizure activity, and developmental delay and personality disorders. Some evidence suggests that severe hypoglycaemia may impair cardiovascular function. Hypoglycaemia had significant association with neonatal risk factors like prematurity and birth weight.[16]

In this study in addition to incident of hypoglycaemia, the symptoms exhibited in neonates during hypoglycaemia (jitteriness, lethargy, convulsion, apnoeic spell) were also identified. Moreover association of hypoglycaemia with neonates with birth asphyxia, sepsis, and hypoglycaemia were also elicited. Added to this the association of hypoglycaemia with type of feed for the neonates and the duration of neonatal unit stay were also identified. For health care professionals the knowledge of neonatal hypoglycaemia and knowing the risk factors and the signs and symptoms will help them to act at once and thus prevent the complications and add an impact on the quality of care to the neonates. Since nurses are primarily taking care of the neonates in neonatal intensive care unit (NICU) round the clock and also involved in planning nursing care for neonates their role includes prevention, detection and treatments of neonatal hypoglycaemia and neonatal hypoglycaemia screening. Knowledge on incidence of neonatal hypoglycaemia and the risk factors will aid them in formulating prevention strategies in neonatal unit. Hence this study is aim to assess the incidence and risk factors of hypoglycaemia.

Materials and Methods

A prospective observational design was adopted for the study to identify the incidence of hypoglycaemia and its determinants among neonates. The study was conducted in NICU of a tertiary care hospital during December 2021 to January 2022. The bed strength of NICU is 60. It has 3 different levels. Level 1 has 31 beds; level 2 has 15 beds and level 3 has 14 beds. In level 1 and 2 mothers are allowed to stay with neonates and in level 3 during visiting time the mothers can see their neonates. Since case method of nursing assignment method is followed in NICU, this aids them in close monitoring of assigned neonates and to detect hypoglycaemic clinical signs and symptoms. Based on prevalence of hypoglycaemia among neonates in NICU as 12% (Jawaharlal institute of postgraduate medical education and research, NICU data) at 5%

absolute precision and 90% confidence level 115 neonates were enrolled in the study. The samples were calculated using the software open epi version 3. Neonates admitted in NICU and whose parents gave willingness to allow their neonates to participate in the study were included in the study. Neonates who expired within first 2 hours of life were excluded from the study. Every day neonates who met the inclusion criteria were selected through convenient sampling method. Informed consent was obtained from parents after explaining the purpose of the study, benefits to the participants, the risks involved, maintenance of confidentiality of the data collected and freedom to withdraw from the study.

Demographic and clinical characteristics of neonates and mothers were collected by interview with mother and from medical record. Neonates were observed daily and hypoglycaemic data was collected. It took 45 minutes for each neonate.

Data collection instrument had three sections. The first section includes clinical and demographic characteristics of the neonates. It comprised of gender, gestational age, birth weight, age, term or preterm, intra uterine growth retardation, small or large for gestation, very low birth weight or extremely low birth weight, history of asphyxia, poor feeding, sepsis, anuria, encephalopathy, respiratory distress syndrome, jaundice, hypothermia, polycythemia, RH incompatibility vomiting, resuscitation at birth and also nutritional data like duration of intravenous fluid, duration of oral feed. It also included respiratory support like duration of mechanical ventilation. It also had duration of NICU stay.

Second section had on maternal clinical characteristics. It comprised of mode of delivery and history of diabetes mellitus, pregnancy induced hypertension, twins and gestational diabetes mellitus. Third section dealt with hypoglycaemia like age (in hours) at which first episode detected, blood glucose value at that time, whether accompanied by symptoms like jitteriness, lethargy or apnoeic spell, whether the neonate had single or multiple episodes of hypoglycaemia.

The content validity of the three sections of the tool was obtained from the experts of neonatology and nursing field. Reliability was examined by Cronbach's alpha (alpha-0.6) for the three sections of the tool.

Data were analysed using statistical package for social sciences (SPSS) version 25. Both descriptive and inferential statistics were used for analysis of data. Descriptive statistics (frequency, percentage) were used to describe the clinical and demographic variables of study participants. Chi-square test was used to identify the association of hypoglycaemia with clinical variables. Logistic regression analysis was used to explore the determinants of hypoglycaemia.

Results

Most of the neonates were male and 36.5% were preterm.

34.8% had low birth weight and mean gestational age was 37.52. About 13.9% had respiratory distress syndrome and 92.2% had less than 5 days of NICU stay. Most of the neonates were born by caesarean section. Twenty-seven percentage and 13% of mother had pregnancy induced hypertension and gestational diabetes mellitus respectively. About 12.2% had twin pregnancy (Table 1).

Table 1 illustrated that majority of the neonates were male and 36.5% were preterm. Their mean gestational age and birth weight were 37.52 and 2311kg respectively. About 14% had respiratory distress syndrome and jaundice. 92.2% had less than 5 days of NICU stay.

Majority of the neonates were delivered by caesarean section.27.8% of mother had pregnancy induced hypertension and 13% had gestational diabetes.

Among 115 neonates 30.4% had hypoglycemia. About 68.5% had single episode of hypoglycemia. Symptoms like jitteriness and lethargy were exhibited in 11.4% and 8.5% respectively (Table 2). There was significant association between hypoglycemia and neonatal categorical clinical characteristics like small for gestation, intra uterine growth retardation, birth asphyxia and history of poor feeding (Table 3).

Table 2 illustrated that 68.5% neonates had single episode of hypoglycaemia and mean lowest blood glucose value recorded was 11.31 mg/dL.

Table 3 Illustrated that there was significant association between hypoglycaemia and neonatal and maternal categorical clinical characteristics like small for gestation, intra uterine growth retardation, birth asphyxia, history of poor feeding and gestational diabetes mellitus.

There was significant association between hypoglycemia and neonatal continuous clinical characteristics like birth weight and length of stay in NICU (Table 4).

Table 4 illustrated that there were significant association between hypoglycaemia and neonatal continuous clinical characteristics like birth weight and length of stay in NICU.

Hypothermia, sepsis, prematurity, small for gestation, intra uterine growth retardation, birth asphyxia. Twin pregnancy were identified as significant determinants of hypoglycemia among neonates (Table 5).

Table 5 illustrated that there was significant association between hypoglycaemia and risk factors such as hypothermia, sepsis, prematurity, and small for gestation, intra uterine growth retardation, and birth asphyxia, twin pregnancy, convulsions and lethargy.

Discussion

This prospective observational study included 115 neonates. The incidence of hypoglycaemia was 30.4%. Similarly a prospective longitudinal study conducted by De et al in India among 150 neonates over a period of six months revealed that 32% had hypoglycaemia.[15] Inconsistent with this an observational study conducted by Thinesh Kumar et al in institute of obstetrics and

Table 1. Distribution of neonatal & maternal clinical characteristics among neonates admitted in NICU (N = 115)

Variable	No. (%)
Gender	
Male	66 (57.4)
Female	49 (42.6)
In determinant	0 (0)
Encephalopathy	
Yes	1 (0.9)
No	114 (99.1)
Neonatal jaundice	
Yes	16 (14)
No	99 (86)
Vomiting	
Yes	1 (0.9)
No	114 (99.1)
Length of stay in NICU	
<5 days	106 (92.2)
>5 days	9 (7.8)
Median length of stay	2 (1-3)
Gestational age in weeks	
<38 weeks	55 (47.8)
>38 weeks	60 (52.2)
Mean gestational age in weeks	37.52 (1.98)
Anuria	
Yes	1 (0.9)
No	114 (99.1)
Prematurity	
Yes	42 (36.5)
No	73 (63.5)
Small for gestation	
Yes	46 (40)
No	69 (60)
Large for gestation	
Yes	9 (7.8)
No	106 (92.2)
Mechanical ventilation	
Yes	1 (0.9)
No	114 (99.1)
Pregnancy induced hypertension	
Yes	32 (27.8)
No	83 (72.2)
Diabetes mellitus	
Yes	4 (3.5)
No	111 (96.5)
Gestational diabetes mellitus	
Yes	15 (13)
No	100 (87)
Respiratory distress syndrome	
Yes	16 (14)

Table 1. Continued.

Variable	No. (%)
No	99 (86)
Rhesus incompatibility	
Yes	1 (0.9
No	114 (99.1)
Right solitary kidney	
Yes	1 (0.9)
No	114 (99.1)
Subgaleal bleed	
Yes	1 (0.9)
No	114 (99.1)
Hypothermia	
Yes	1 (0.9)
No	114 (99.1)
Birth weight	
Extremely low birth weight	4 (3.5)
Very low birth weight	15 (13)
Low birth weight	40 (34.8)
Normal birth weight	56 (48.7)
Mean birth weight	2311.58±757.9
IUGR-Intrauterine growth retardation	
Yes	3 (2.6)
No	112 (97.4
Birth asphyxia	
Yes	3 (2.6)
No	112 (97.4)
History of poor feeding	
Yes	9 (7.8)
No	106 (92.2)
Nutrition	
Oral feeds	106 (92.2)
Twin pregnancy	
Yes	14 (12.2)
No	101 (87.8)

Table 2. Distribution of hypoglycemia among neonates (N = 35)

Hypoglycemia	No. (%)
Episode(single)	24 (68.5)
(Multiple)	11 (31.4)
Mean (SD) Lowest blood glucose value recorded	11.31 (17.91)
Mean (SD) age at which first episode occurred hypoglycemia detected in hours	6.33 (16.05)
Jitteriness	
Yes	4 (11.4)
No	31 (88.5)
Convulsions	
Yes	1 (2.8)
No	34 (97.1)
Apneic spells	
Yes	0 (0)
No	35 (100)
Lethargy	
Yes	3 (8.5)
No	32 (91.4)

gynaecology, among 1883 neonates showed that 33.3% had hypoglycaemia.[17] A prospective longitudinal study conducted from October 2017 to October 2018 among 50 neonates reported 30% of hypoglycaemia.[14] Furthermore a longitudinal study among 100 neonates showed the incidence of hypoglycaemia as 15%.[18] In addition to this a study conducted in Tehran from June 2004 to march 2005 identified the incidence of hypoglycaemia as 15.15%.[19] Similarly a study carried out by Ali et al from May 2019 to December 2019 among 398 neonates showed 10.55% hypoglycaemia.[20] In consistent with this a longitudinal study conducted in Bangalore among 100 neonates revealed that the incidence of hypoglycaemia was 10%.[10] In addition to this a prospective case-control study done in Bangladesh among 186 neonates revealed that the incidence of hypoglycaemia was 17.2 %.[16] In contrast to this a study has reported the incidence was only 8.26%.[21]

Among 30.4% of hypoglycaemia 68.5% had single episode and 31.4% had multiple episodes. Similarly, a prospective observational study conducted from September 2011 to September 2012 among 407 newborns also revealed that only 32.7% had multiple episodes.[22] In current study mean (SD) age at which first episode of hypoglycaemia detected was 6.33(16.05) hours. In consistent with this Thinesh Kumar et al concluded that 31% of neonates had hypoglycaemia at 6 hours of life.[17] In addition to this a study has revealed that 21.8% had hypoglycaemia at first 6 hours of life.[22] In line with these results during first 2 to 6 hours 8.33% had hypoglycaemia.[23] Another study supported this and showed that episodes of hypoglycaemia occurred during first 24 hours of life.[20]

Among the symptoms of hypoglycaemia 11.4% exhibited with jitteriness. Similarly a prospective observational study revealed that 11.9% had jitteriness.[24] A study has reported that 7% had jitteriness.[20] In contrast to this studies reported 55.5%, 48%, 37.5% and 41% respectively.[18,21,22,25] Only 2.8% exhibited convulsions in current study. In contrast to this studies by Dashti et al, Babu et al, Somanathan et al and Nishikant et al reported 30%, 22.22%, 16.6% and 9.5% respectively.[19,21,24,25] Among the symptoms of hypoglycaemia none had apnoeic spell. In consistent with this a study reported that none had apnoeic spell.[18] In contrast to this studies by Dashti et al, Babu et al and Nishikant et al showed 9.8%, 16.66% and 9.8% respectively.[19,21,25] In current study only 8.5% exhibited lethargy as one of the symptoms of hypoglycaemia. Contradicting this some studies showed 64%, 19.05%, 58%, 40%17.8% and 25% respectively.[18,21-23,25,26]

In current study there was no significant association

Table 3. Association between hypoglycemia and neonatal and maternal risk factors (categorical variables) among neonates (N = 115)

Neonatal clinical characteristics	Hypoglycemia, No. (%)		χ²	df	P value²
	Yes	No			
Gender					
Male	20 (57.1)	46 (57.5)	0.001	1	0.972
Female	15 (42.9)	34 (42.5)			
Hypothermia					
Yes	1 (2.9)	0 (0%)	2.306	1	0.129
No	34 (97.1)	80 (100)			
Sepsis					
Yes	1 (2.9)	0 (0%)	2.306	1	0.129
No	34 (97.1)	80 (100)			
Prematurity					
Yes	17 (48.6)	25 (31.3)	3.151	1	0.076
No	18 (51.4)	55 (68.8)			
Small for gestation					
Yes	24 (68.6)	22 (27.5)	17.113	1	0.000*
No	11 (31.4)	58 (72.5)			
Large for gestation					
Yes	2 (5.7)	7 (8.8)	0.311	1	0.577
No	33 (94.3)	73 (91.3)			
Intra uterine growth retardation					
Yes	3 (8.6)	0 (0)	7.041	1	0.008*
No	32 (91.4)	80 (100)			
Birth asphyxia					
Yes	3 (8.6)	0 (0)	7.014	1	0.008*
No	32 (91.4)	80 (100)			
History of poor feeding					
Yes	8 (22.9)	1 (1.3)	15.758	1	0.000*
No	27 (77.1)	79 (98.8)			
Nutrition					
Oral feeds	30 (85.7)	76 (95)			
Intravenous fluid	2 (5.7)	1 (1.3)	3.173		0.205
Both	3 (8.6)	3 (3.8)			
Mechanical ventilation					
Yes	0 (0)	1 (1.3)	0.441		0.506
No	35 (100)	80 (100)			
Pregnancy induced hypertension					
Yes	12 (34.3)	20 (25)	1.045	1	0.307
No	23 (65.7)	60 (75)			
Diabetes mellitus					
Yes	1 (2.9)	3 (3.8)	0.058	1	0.810
No	34 (97.1)	77 (96.3)			
Gestational diabetes mellitus					
Yes	10 (28.6)	5 (63)	10.969	1	0.001*
No	25 (71.4)	75 (93.8)			
Twin pregnancy					
Yes	6 (17.1)	8 (10.1)	3.58	2	0.16
No	28 (80)	72 (90)			
Mode of delivery					
Assisted breech delivery	2 (5.7)	0 (0)			
Spontaneous vaginal delivery	15 (42.9)	30 (37.5)	6.83	3	0.07
Instrumental	4 (11.4)	5 (6.3)			
Caesarean section	14 (40)	45 (56.3)			

ᵃChi-square test; *Statistically significant.

Table 4. Association between hypoglycaemia and neonatal risk factors (continuous variables) (N = 115)

Hypoglycemia	Mean (SD)	T value	P valueᵃ
Length of stay in NICU			
Present	3.17 (2.69)	-2.051	0.043*
Absent	2.26 (1.92)		
Gestational age			
Present	37.01 (2.28)	1.842	0.068
Absent	7.74 (1.81)		
Age			
Present	3.66 (2.95)	-0.899	0.371
Absent	3.13 (2.90)		
Birth weight			
Present	2018.66 (589.58)	2.824	0.006*
Absent	2439.74 (790.37)		

ᵃ Independent t test; *Statistically significant.

between hypoglycaemia and neonates gender. In consistent with this a prospective descriptive study conducted also showed no significance = 0.72.[26] In addition to this a study also showed non significance $P = 0.714$.[27] In contrast to this a study has reported significant association.[22] Prematurity had no significant association with hypoglycaemia. Similarly an observational study conducted at Skopje, Macedonia among 84 neonates also showed non significance.[28] In contrary to the above results some studies showed significant association $P < 0.001$, $P = 0.005$ and $P = 0.022$ respectively.[16,26,27] Small for gestation had significant association with hypoglycaemia. In consistent with this a study also revealed significant association $P < 0.001$.[16] Contradicting this a study showed nonsignificant.[26] Large for gestation had no significant association with hypoglycaemia. Similarly a study also showed non significance.[26] Contradicting this a study revealed significance $P < 0.001$.[16] Birth asphyxia had significant association with hypoglycaemia. In accordance with this a research also reported significance $P = 0.02$[16] In contrast to this a study showed non significance $P = 1.000$.[26] Birth weight showed significant association with hypoglycaemia. In consistent with this a study revealed significant association $P = 0.003$.[22]

Among the maternal risk factors pregnancy induced hypertension had no significant association with hypoglycaemia. Similarly a study also showed non significance $P = 0.801$.[26] Diabetes mellitus also not had significant association with hypoglycaemia which is similar to the findings of a study in which $P = 1.000$.[26] Gestational diabetes had significant association with hypoglycaemia. In consistent with this some studies revealed significant association $P = 0.006$ and $P < 0.001$ respectively.[16,27] Mode of delivery had no significant association with hypoglycaemia. Congruently research showed nonsignificance.[16]

The goal of treating hypoglycaemia is to prevent

Table 5. To identify risk factors associated with hypoglycemia in neonates (N = 115)

Variables	Odds Ratio	Standard error	Z	P value[a]	95% CI	
					Lower	Upper
Gender	-0.014	0.039	-0.355	0.723	-0.092	0.064
Length of NICU stay	-0.107	0.088	-1.214	0.228	-0.283	0.068
Gestational age	-0.008	0.068	-0.124	0.901	-0.143	0.126
Age at months	0.063	0.042	1.493	0.139	-0.021	0.146
Birth weight	-0.032	0.041	-0.773	0.442	-0.114	0.050
Hypothermia	1.591	0.315	5.059	0.000*	0.966	2.216
Sepsis	1.033	0.308	3.359	0.001*	0.422	1.644
Prematurity	0.225	0.076	2.975	0.004*	0.075	0.375
Small for gestation	-0.269	0.075	-3.560	0.001*	-0.418	-0.119
Large for gestation	0.009	.087	0.099	0.922	-0.163	0.180
Intra uterine growth retardation	0.302	0.127	2.380	0.019*	0.050	0.553
Birth asphyxia	-2.114	0.240	-8.823	0.000*	-2.591	-1.638
History of poor feeding	0.117	0.096	1.212	0.229	-0.075	0.308
Nutrition	0.020	0.057	0.356	0.723	-0.094	0.134
Pregnancy induced hypertension	-0.051	0.051	-0.996	0.322	-0.152	0.050
Diabetes mellitus	-0.020	0.133	-0.153	0.879	-0.284	0.243
Gestational diabetes mellitus	-0.063	0.070	-0.894	0.374	-0.202	0.077
Twin pregnancy	0.157	0.072	2.173	0.032*	0.013	0.301
Mode of delivery	0.031	0.023	1.325	0.189	-0.015	0.076
Jitteriness	0.108	0.128	0.843	0.401	-0.146	0.362
Convulsions	-2.605	0.392	-6.648	0.000*	-3.383	-1.826
Lethargy	1.230	0.281	4.384	0.000*	0.672	1.787

[a] Logistic regression, *Statistically significant.

or to minimize brain injury by maintaining a glucose concentration above an acceptable threshold.[29] A observational prospective study done among 299 exclusively breast-fed neonates reported that 20.06% were hypoglycemic.[30] It has to be mentioned that extreme caution should exercised in generalizing the findings of the study to other populations because the current study was conducted in one region only. Similar study can be carried out with larger sample size. NICU nurses play a significant role in routine assessment of neonates in order to identify the risk factors of hypoglycaemia and to give prompt care.

Conclusion
The findings of this study showed that 30.4% of neonates had hypoglycaemia. At present the universal screening of neonates for hypoglycaemia is not recommended. The issue needs to be addressed as unrecognised hypoglycaemia may result in long term neurological sequelae.

Author's Contribution
Conceptualization: Vetriselvi Prabakaran, Indumathi Manoharan, Adhisivam Bethou.
Data curation: Vetriselvi Prabakaran, Indumathi Manoharan, Adhisivam Bethou.
Formal analysis: Vetriselvi Prabakaran, Indumathi Manoharan, Adhisivam Bethou.
Investigation: Vetriselvi Prabakaran, Indumathi Manoharan.
Methodology: Vetriselvi Prabakaran, Indumathi Manoharan, Adhisivam Bethou.
Project administration: Vetriselvi Prabakaran, Indumathi Manoharan, Adhisivam Bethou.
Supervision: Vetriselvi Prabakaran, Indumathi Manoharan.
Validation: Vetriselvi Prabakaran, Adhisivam Bethou.
Writing-original draft: Vetriselvi Prabakaran, Indumathi Manoharan, Adhisivam Bethou.
Writing-review & editing: Vetriselvi Prabakaran, Indumathi Manoharan, Adhisivam Bethou.

Data Availability Statement
The datasets are available from the corresponding author on reasonable request.

Ethical Approval
The current study is a part of master of science in paediatric nursing thesis approved by Nursing Research Monitoring Committee (JIP/CON/NRMC/M.Sc./2020/PN/2) and Ethics Committee (JIP/CON/IEC/M.Sc./2020/PN/2).

Research Highlights

What is the current knowledge?

- In NICU vigilant observation and blood glucose monitoring is routine for Preterm neonates, small for gestational neonates and neonates of diabetes mothers since they are more prone for hypoglycemia.

What is new here?

- In this study neonates who had birth asphyxia, sepsis and hypothermia are also exhibited with episodes of hypoglycemia.
- Moreover 85.7% of neonates who had oral feeds also had hypoglycemia.
- Mean age of first episode of hypoglycemia was detected at 6 hours of age and 77.3% of neonates not showed any physical symptoms.
- These findings throw a light on modification of NICU protocols to monitor blood glucose levels among neonates.

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