

## Original research article

## Prospective observational study to determine the clinical profile of hypoglycemia in newborn and to determine the prevalence of hypoglycemia among neonates admitted in NICU

Dr. Pankaj Kumar Kashyap<sup>1</sup>, Dr. Gopal Sharan<sup>2</sup>

<sup>1</sup>Senior Resident, Upgraded Department of Paediatrics, Patna Medical College & Hospital, Patna, Bihar, India.

<sup>2</sup>Professor, Upgraded Department of Paediatrics, Patna Medical College & Hospital, Patna, Bihar, India.

Corresponding Author: Dr. Pankaj Kumar Kashyap

### Abstract

**Aim:** to determine the clinical profile of hypoglycemia in newborn and to determine the prevalence of hypoglycemia among neonates admitted in NICU.

**Material and methods:** This prospective observational study was done the Upgraded Department of Paediatrics, Patna Medical College & Hospital, Patna, Bihar, India, for July 2017 to July 2018. 120 Patients admitted in NICU with blood glucose less than 45 mg/dl were included in this study. In neonates with risk factors blood sugar was screened at 2, 6, 12, 24, 48 and 72 hours of life or whenever symptoms suggestive of hypoglycemia developed in any neonates and for critically sick neonates blood sugar was screened in every 6 hour in active phase of illness.

**Results:** The total number of admissions in NICU during the study period was 720 and among them the prevalence of hypoglycemia was 120 (16.67%). Among the 120 neonates with hypoglycemia, 70 (58.33%) were males and 50 (41.67%) were females. Among the study population 104 (86.67%) of neonates had at least one risk factor (maternal/neonatal) and 16 cases (13.33%) had no risk factor. The maternal risk factors that were associated with hypoglycemia were GDM, PIH, PROM. 19.17% had GDM, 11.67% had PIH and 2.5% had PROM as maternal risk factors. 66.67% had no maternal risk factor. The neonatal risk factors associated with hypoglycemia were prematurity 33(27.5%), SGA 38(31.67%), LGA 8(6.67%), IDM 26(21.67%) and comorbidities (sepsis, birth asphyxia, polycythemia and shock) were present in 21(17.5%) of the hypoglycemic neonates. Among the comorbid condition birth asphyxia was present in 8 (6.67%), sepsis in 9(7.5%), polycythemia in 3(2.5%) and shock in 1 (0.83%). 86.67% of the hypoglycemic neonates had at least one risk factor. Out of 120 children with hypoglycemia 78 (65%) were asymptomatic and 42 (35%) presented with symptoms. The common symptoms were poor feeding (66.67%), lethargy (19.05%), jitteriness (4.17%), irritability (2.5%), hypotonia (0.83%) and cyanosis (0.83%). 31.67% of neonates presented with hypoglycemia on day 1 of life, 25% of neonates on day 2, 20.83% on day 3 and 22.5% beyond 72 hours of life.

**Conclusion:** Blood glucose screening in neonates with this risk factor is mandatory as many of the neonates were asymptomatic. The importance of early initiation of breast feeding to prevent hypoglycemia should be emphasized.

**Keywords:** Clinical profile, Hypoglycemia, Neonates, Prevalence, Risk factor

### Introduction

Hypoglycemia is one of the commonest metabolic problems in contemporary neonatal medicine. In the majority of healthy neonates, the frequently observed low blood glucose

concentrations are not related to any significant problem and merely reflect normal processes of metabolic adaptation to extra uterine life. However, when low blood glucose levels are prolonged or recurrent, they may result in acute systemic effects and neurologic sequelae.<sup>1</sup> The fetus in utero is entirely dependent on the mother for glucose. At the time of birth, the neonate must abruptly switch from having a continuous supply of glucose from the maternal blood in fetal life to maintaining its own supply of glucose during periods of fasting, and when feedings are interspersed intermittently.<sup>2</sup> Neonatal hypoglycemia may be symptomatic and asymptomatic. Hypoglycemic neonates commonly present with refusal to feed, apathy jitteriness, convulsions, hypothermia, cyanosis and respiratory abnormality. After clinical evaluation hypoglycemia should always be confirmed by blood glucose estimation and response to treatment. Undiagnosed hypoglycemia can have long term neurological consequences; thus, the emphasis is on prevention and early detection along with treatment of asymptomatic hypoglycemia.<sup>3-4</sup> Due to lack of significant correlation among plasma glucose concentration, clinical symptoms and long-term sequelae, definition of hypoglycemia in the newborn infant has remained controversial. Currently, the operational threshold for hypoglycemia is blood glucose value of < 40 mg/dl or plasma glucose < 45 mg/dl, in symptomatic newborn with plasma glucose < 45 mg/dl clinical interventions are indicated to increase blood glucose levels and in asymptomatic neonate with plasma glucose < 36 mg/dl surveillance of glucose levels should be done and intervention is required if symptoms appear or level do not increase after feeding.<sup>5,6</sup> Even after many years of research and debate there is limited evidence-based consensus regarding screening and management of neonates at risk of hypoglycemia, the dilemma exists.

Neonatal hypoglycaemia can be easily treated if recognized early. Untreated hypoglycaemia whether symptomatic or asymptomatic results in neurological impairment and mental retardation of varied severity.<sup>7,8</sup> The aim of the present study determine the clinical profile of hypoglycemia in newborn and to determine the prevalence of hypoglycemia among neonates admitted in NICU.

### **Material and methods**

This prospective observational study was done the Upgraded Department of Paediatrics, Patna Medical College & Hospital, Patna, Bihar, India, from July 2017 to July 2018, after taking the approval of the protocol review committee and institutional ethics committee. 120 newborns with hypoglycemia admitted in NICU were included in this study.

### **Inclusion criteria**

Patients admitted in NICU with blood glucose less than 45 mg/dl were included

### **Exclusion criteria**

Newborns with persistent hypoglycemia which require enzyme and genetic evaluation.

### **Methodology**

In neonates with risk factors blood sugar was screened at 2, 6, 12, 24, 48 and 72 hours of life or whenever symptoms suggestive of hypoglycemia developed in any neonates and for critically sick neonates blood sugar was screened in every 6 hour in active phase of illness. Any neonate with blood glucose level less than 45 mg/dl were analyzed for maternal risk factors, neonatal risk factors and course in the NICU.

### **Results**

The total number of admissions in NICU during the study period was 720 and among them the prevalence of hypoglycemia was 120 (16.67%). Among the 120 neonates with hypoglycemia, 70 (58.33%) were males and 50 (41.67%) were females. Among the study population 104 (86.67%) of neonates had at least one risk factor (maternal/neonatal) and 16 cases (13.33%) had no risk factor.

**Table 1: Descriptive analysis of maternal risk factors in the study population**

Maternal risk factors	Frequency	Percentage
GDM/overt DM	23	19.17
PIH	14	11.67
PROM>18 hours	3	2.5
No risk factors	80	66.67

The maternal risk factors that were associated with hypoglycemia were GDM, PIH, PROM. 19.17% had GDM, 11.67% had PIH and 2.5% had PROM as maternal risk factors. 66.67% had no maternal risk factor (Table 1)

The neonatal risk factors associated with hypoglycemia were prematurity 33(27.5%), SGA 38(31.67%), LGA 8(6.67%), IDM 26(21.67%) and comorbidities (sepsis, birth asphyxia, polycythemia and shock) were present in 21(17.5%) of the hypoglycemic neonates. Among the comorbid condition birth asphyxia was present in 8 (6.67%), sepsis in 9(7.5%), polycythemia in 3(2.5%) and shock in 1 (0.83%). 86.67% of the hypoglycemic neonates had at least one risk factor (Table 2).

**Table 2: Descriptive analysis of neonatal risk factors in the study population**

Neonatal risk factors	Frequency	Percentage
Preterm <37 weeks	33	27.5
SGA	38	31.67
LGA	8	6.67
IDM	26	21.67
Associated comorbidities	21	17.5
Nil	16	13.33

Out of 120 children with hypoglycemia 78 (65%) were asymptomatic and 42 (35%) presented with symptoms. The common symptoms were poor feeding (66.67%), lethargy (19.05%), jitteriness (4.17%), irritability (2.5%), hypotonia (0.83%) and cyanosis (0.83%). 31.67% of neonates presented with hypoglycemia on day 1 of life, 25% of neonates on day 2, 20.83% on day 3 and 22.5% beyond 72 hours of life (Table 3).

**Table 3: Descriptive analysis of clinical features in the study population**

Clinical Features	Frequency	Percentage
Irritability	3	2.5
Poor feeding	20	16.67
Jitteriness	5	4.17
Seizures	4	3.33
Lethargy	1	0.83
Lethargy, poor feeding	7	5.83
Hypotonia, poor feeding	1	0.83
Cyanosis	1	0.83
No symptoms	78	65

**Table 4: Time of detection of hypoglycemia in the study population**

Time of detection	Frequency	Percentage
2-6 hours	10	8.33
6-12 hours	12	10
12-24 hours	16	13.33
24-48 hours	30	25
48-72 hours	25	20.83
>72 hours	27	22.5

The time for detection of hypoglycemia in newborn were 2-6 hours in 10 (8.33%), 6-12 hours in 12(10%), 12-24 hours in 16 (13.33%), 24-48 hours in 30 (25%), 48-72 hours in 25 (20.83%) and >72 hours in 27(22.5%) of cases. table 4.

In our study 87 (72.5%) neonates required oral feeds (EBM) for the correction of hypoglycemia, 31 (25.83%) required i.v. dextrose and 2 (1.67%) neonate required hydrocortisone.

Out of 120 neonates 10 (8.33%) neonates attained euglycemia within 30 minutes, 91(75.83%) in 1 hour, 13(10.83%) in 2 hours, 4 (3.33%) within 2-6 hours and 2 (1.67%) neonates required 6-12 hours to attain euglycemia. Out of 120 neonates 70 (58.33%) required 24 hours of hospital stay, 14 (11.67%) required 24-48 hours, 16(13.33%) required 48-72 hours, and 20(16.67%) required more than 72 hours of NICU stay. In the present study 116 (96.67%) neonates recovered and mortality was in 4 (3.33%) neonates. All these neonates had become euglycemic following treatment but had expired because of the co-morbidities.

### Discussion

In the present study among the 120 neonates with hypoglycemia, 70 (58.33%) were males and 50 (41.67%) were females. This was similar to the study conducted by Dhananjaya et al, Singh et al, Babu MR et al.<sup>9-11</sup>

Most neonates with hypoglycemia had maternal risk factors such as 19.17% had GDM, 11.67% had PIH and 2.5% had PROM as maternal risk factors. 66.67% had no maternal risk factor.

The percentage of GDM as a risk factor in hypoglycemic newborn (19.17%) in the present study was similar to that of Singhal et al (23.8%), because of the similar inclusion criteria for GDM.<sup>12</sup> In the study by Babu et al, percentage of GDM (5%) as a risk factor in hypoglycemic newborn was comparatively low because of difference in inclusion criteria such as exclusion of pre-gestational DM and mothers on OHA.<sup>11</sup> PIH was a risk factor in study conducted by Singh et al (11%) which is similar to the current study (11.67%).<sup>10</sup> Percentage of PROM was very less (2.5%) when compared to other studies like Singh et al (8.5%), Amarendra et al (15.3%) as we taken PROM more than 18 hours as a risk factor.<sup>10,13</sup>

In present study the neonatal risk factors associated with hypoglycemia were prematurity 33(27.5%), SGA 38(31.67%), LGA 8(6.67%), IDM 26(21.67%) and comorbidities (sepsis, birth asphyxia, polycythemia and shock) were present in 21(17.5%) of the hypoglycemic neonates. Among the comorbid condition birth asphyxia was present in 8 (6.67%), sepsis in 9(7.5%), polycythemia in 3(2.5%) and shock in 1 (0.83%). 86.67% of the hypoglycemic neonates had at least one risk factor. Other studies showed incidence as follows, Singhal et al (12.8%), Singh et al (46%), Dhananjaya et al (11.9%).<sup>9,10,12</sup> SGA contributes 31.67% hypoglycemic babies in the present study which is similar to studies conducted by Singhal et al (17%), Singh et al (23.5%), Anjum et al (29%).<sup>10,12,14</sup> LGA contributes 6.67% of hypoglycemia in the present study which is similar to other studies by Singh et al (4.5%), Holtrope et al (5%).<sup>10,15</sup> 17.5% neonates had associated comorbid conditions. Among them perinatal asphyxia accounts for 6.67%, sepsis 7.5%, polycythemia 2.5% and shock 0.83%. 86.67% neonates had at least one single risk factor similar to the study conducted by Sashidaran et al (89.1%).<sup>16</sup>

Out of 120 children with hypoglycemia 78 (65%) were asymptomatic and 42 (35%) presented with symptoms. This was similar to the studies conducted by Singh et al, Singhal et al, Amerandra et al.<sup>10,12,13</sup> The common symptoms were poor feeding (66.67%), lethargy (19.05%), jitteriness (4.17%), irritability (2.5%), hypotonia (0.83%) and cyanosis (0.83%). 31.67% of neonates presented with hypoglycemia on day 1 of life, 25% of neonates on day 2, 20.83% on day 3 and 22.5% beyond 72 hours of life. In Dhananjaya et al majority of the newborn (55.26%) were found to be hypoglycemic in day 2 of life.<sup>9</sup> The percentage of hypoglycemia in Amarendra et al was very high in the first 24 hours (86.11%).<sup>13</sup> In our study 87 (72.5%) neonates required oral feeds (EBM) for the correction of hypoglycemia, 31 (25.83%) required i.v. dextrose and 2 (1.67%) neonate required hydrocortisone. Results were varied from the study done by Singh et al which showed 34% hypoglycemia required oral feeds and 66% required i.v. fluids.<sup>10</sup> Out of 120 neonates 10 (8.33%) neonates attained euglycemia within 30 minutes, 91(75.83%) in 1 hour, 13(10.83%) in 2 hours, 4 (3.33%) within 2-6 hours and 2 (1.67%) neonates required 6-12 hours to attain euglycemia. Out of 120 neonates 70 (58.33%) required 24 hours of hospital stay, 14 (11.67%) required 24-48 hours, 16(13.33%) required 48-72 hours, and 20(16.67%) required more than 72 hours of NICU stay. In the present study 116 (96.67%) neonates recovered and mortality was in 4 (3.33%) neonates. 96.67% neonates with hypoglycemia were recovered similar to the studies done by Singh et al (90.2%).<sup>10</sup> Neonatal mortality was 3.33% in present study, the most common causes of neonatal deaths were not due to hypoglycemia per se but due to co morbid conditions like birth asphyxia, extreme prematurity with respiratory distress syndrome, sepsis, meconium aspiration syndrome with PPHN.

This study has some limitations. The study group included only neonates admitted in NICU and not all neonates delivered in the hospital, so the data may not represent the entire population. Outborn babies were also not included. Neonates with persistent hypoglycemia were excluded from the study due to non-availability of the investigations. Neurodevelopmental outcome in these babies on follow up were not assessed in the present study. A prospective study with larger sample size incorporating these limitations would be ideal

### Conclusion

Blood glucose screening in neonates with this risk factor is mandatory as many of the neonates were asymptomatic. The importance of early initiation of breast feeding to prevent hypoglycemia should be emphasized.

### Reference

1. Cornblath M, Hawdon JM, Williams AF, Aynsley-green A, Ward-platt MP, et al. Controversies regarding definition of neonatal hypoglycemia : Suggested operational thresholds. *Pediatrics*.2000;105: 1141-1145.
2. Murty VY, Ram KD. Study of pattern of blood sugar levels in low birth weight babies who are exclusively on breast milk. *J Dr NTR Univ Heal Sci*.2012;1: 90-93
3. Kliegman RM. Problems in metabolic adaptation: glucose, calcium, and magnesium. In: *Care of the highrisk neonate*. 5 th edition. Saunders; 2001:301.
4. Barbara JS, Robert MK. The Endocrine System. In: Behrman RE, Kliegman RM, Jenson HB, eds. *Nelson Text Book of Pediatrics*. 17th ed. Philadelphia: Saunders; 2004:614-616.
5. De AK, Biswas R, Samanta M, Kundu CK. Study of blood glucose level in normal and low birth weight newborn and impact of early breast feeding in a tertiary care centre. *Ann Nigerian Med*. 2011;5(2):53.
6. Heck LJ, Erenberg A. Serum glucose levels in term neonates during the first 48 hours of life. *J Pediatr*. 1987;110(1):119-22.

7. Platt MW, Deshpande S. Metabolic adaptation at birth. *Semin Fet Neonat Med.* 2005;10(4):341-50.
8. Dean AG, Sullivan KM, Soe MM. Open Epi: Open Source Epidemiologic Statistics for Public Health, Version 3.01. Available from: [https://www.openepi.com/Menu/OE\\_Menu.htm](https://www.openepi.com/Menu/OE_Menu.htm). Accessed on 16 August 2015.
9. Dhananjaya CD, Kiran B. Clinical profile of hypoglycemia in newborn babies in a rural hospital setting. *Int J Biol Med Res.* 2011;2(4):1110-4.
10. Singh K, Kher AM. Clinico-biochemical profile of hypoglycemia in neonates admitted in NICU. *Int J Contemp Pediatr.* 2015;6(1):1.
11. Babu MR, D'Souza JL, Susheela C. Study of incidence, clinical profile and risk factors of neonatal hypoglycemia in a tertiary care hospital. *Int J Pediatr Res.* 2016;3(10):753.
12. Singhal PK, Singh M, Paul VK, Deorari AK, Ghorpade MG, Malhotra A. Neonatal hypoglycemia--clinical profile and glucose requirements. *Indian Pediatr.* 1992;29(2): 167-71.
13. Amarendra M, Sethi RK, Pericherla VP. Incidence of hypoglycemia within 72 hours after birth in low birth weight babies who are appropriate for gestational age. *Int J Contemp Paediatr.* 2018;5(3):944.
14. Anjum R, Anjum R, Qayum S. Neonatal hypoglycemia: risk factors and clinical profile. *J Med Sci Clin Res.* 2014;7(2):1081-5
15. Holtrop PC. The frequency of hypoglycemia in full- term large and small for gestational age newborns. *Am J Perinatol.* 1993;10(02):150-4.
16. Sasidharan CK, Gokul E, Sabitha S. Incidence and risk factors for neonatal hypoglycemia in Kerala, India. *Ceylon Med J.* 2010;49(4).

Received :13-05-2020 Revised: 11-06-2020. Accepted:10-07-2020