A Hospital-Based Prospective Study: To Assess the Prevalence and Risk Factors of Neonatal Hypoglycemia

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Abstract

Aim: The aim of the present study is to determine the Incidence and risk factors of hypoglycemia among neonates. **Methods:** This prospective observational study was done in the Department of Pediatrics, Nalanda Medical College and Hospital, Patna,Bihar, India, from January 2020 to March 2021. 110 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 neonate. For critically sick neonate blood sugar was screened in every 6 hours in active phase of illness. **Results:** The total number of admissions in NICU during the study period was 680 and among them the prevalence of hypoglycemia was 110 (15.94%). Among the 110 neonates with hypoglycemia, 66 (60%) were male and 54 (40%) were female. Among the study population 97 (88.18%) of neonates had at least one risk factor (maternal/neonatal) and 13 cases (11.82%) had no risk factor. The maternal risk factors that were associated with hypoglycemia were GDM, PIH, PROM. Maternal age and drug intake. 18.18% had GDM, 10.90% had PIH and 1.82% had PROM as maternal risk factors. 68.18% had no maternal risk factor. The neonatal risk factors associated with hypoglycemia were prematurity 21(28.18%), SGA 36(32.73%), LGA 7(6.36%), IDM 24(21.18%) and comorbidities (sepsis, birth asphyxia, polycythemia and shock) were present in 19(17.27%) of the hypoglycemic neonates. Among the comorbid condition birth asphyxia was present in 7 (6.64%), sepsis in 8(7.27%), polycythemia in 3(2.73%) and shock in 1 (0.91%). 82.73% of the hypoglycemic neonates had at least one risk factor. Out of 110 neonates 9 (8.18%) neonates

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attained euglycemia within 30 minutes, 85(77.27%) in 1 hour, 11(10%) in 2 hours, 3 (2.73%) within 2-6 hours and 2 (1.82%) neonates required 6-12 hours to attain euglycemia. Out of 110 neonates 65 (59.09%) required 24 hours of hospital stay, 13 (11.82%) required 24-48 hours, 15(13.64%) required 48-72 hours, and 17(15.45%) required more than 72 hours of NICU stay. In the present study 106 (96.36%) neonates recovered and mortality was observed in 4 (3.64%) neonates. **Conclusion:** Blood glucose screening in neonates with 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: Locking Plate, Tibia Fractures, Intermedullary Nailing

Introduction

Neonatal hypoglycemia has been recognized for many years, although with time there have been wide swings of opinion regarding the definition of the condition, its clinical significance and its optimal management. For example, in the era when routine postnatal management involved the withholding of feeds from healthy infants for up to 24 hours, even longer in sick or smaller babies, many were found to have low blood glucose concentrations, and this became accepted as a normal finding[1]. Hypoglycemia is the most common but preventable metabolic abnormality in neonates. Prolong neonatal hypoglycemia may result in irreversible brain damage, mental retardation, recurrent seizure activity, personality disorders, and even death. The pathological changes are characterized by atrophic gyri, reduced myelination, and atrophy of cerebral white matter[2]. Blood glucose is essential for normal neurological function and development. Poor reserve of liver glycogen and fat and immature metabolic pathway at birth predisposes preterm and small for gestational age (SGA) neonates to prolonged hypoglycaemia[2-4]. In perinatal asphyxia, high fuel requirement of anaerobic metabolism, the depletion of stores, and a delay in metabolic adaptation are possible underlying mechanisms of hypoglycemia. Neonatal hyperinsulinism and hypoglycemia occur in infants of diabetic mothers (IDMs). Other known causes of neonatal hypoglycemia are islet cell dysregulation syndrome (nesidioblastosis), Beckwith Wiedemann syndrome, insulin-secreting adenoma, congenital hypopituitarism, glycogen storage diseases, defects of amino acids metabolism, defects of gluconeogenesis, and defects of β-oxidation of fatty acids[5-7].

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[8]. 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 in NICU of the Department of Pediatrics, Nalanda Medical College and Hospital, Patna,Bihar, India, from January 2020 to March 2021,after taking the approval of the protocol review committee and institutional

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ethics committee. 110 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.

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 hours in active phase of illness. Any neonate with blood glucose level less than 45 mg/dl was 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 680 and among them the prevalence of hypoglycemia was 110 (15.94%). Among the 110 neonates with hypoglycemia, 66 (60%) were male and 54 (40%) were female. Among the study population 97 (88.18%) of neonates had at least one risk factor (maternal/neonatal) and 13 cases (11.82%) had no risk factor.

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

Maternal risk factors	Frequency	Percentage
GDM/overt DM	20	18.18
PIH	12	10.90
PROM>18 hours	3	1.82
No risk factors	75	68.18

The maternal risk factors that were associated with hypoglycemia were GDM, PIH, PROM. 18.18% had GDM, 10.90% had PIH and 1.82% had PROM as maternal risk factors. 68.18% had no maternal risk factor (Table 1)

The neonatal risk factors associated with hypoglycemia were prematurity 21(28.18%), SGA 36(32.73%), LGA 7(6.36%), IDM 24(21.18%) and comorbidities (sepsis, birth asphyxia, polycythemia and shock) were present in 19(17.27%) of the hypoglycemic neonates. Among the comorbid condition birth asphyxia was present in 7 (6.64%), sepsis in 8(7.27%), polycythemia in 3(2.73%) and shock in 1 (0.91%). 82.73% of the hypoglycemic neonates had at least one risk factor (Table2).

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

Neonatal risk factors	Frequency	Percentage
Preterm <37 weeks	31	28.18
SGA	36	32.73
LGA	7	6.36
IDM	24	21.18
Associated comorbidities	19	17.27
Nil	15	13.64

Out of 110 children with hypoglycemia 74 (67.27%) were asymptomatic and 36 (32.73%) presented with symptoms. The common symptoms were poor feeding (15.45%), lethargy (0.91%), jitteriness (3.64%), irritability (2.73%), hypotonia (0.91%) and cyanosis (0.91%). 30% of neonates presented with hypoglycemia on day 1 of life, 24.55% of neonates on day 2, 21.82% on day 3 and 23.64% beyond 72 hours of life (Table 3)

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

Clinical Features	Frequency	Percentage
Irritability	3	2.73
Poor feeding	17	15.45
Jitteriness	4	3.64
Seizures	3	2.73
Lethargy	1	0.91
Lethargy, poor feeding	6	5.45
Hypotonia, poor feeding	1	0.91
Cyanosis	1	0.91
No symptoms	74	67.27

Table 4 Time of detection of hypoglycemia in the study population

Time of detection	Frequency	Percentage
2-6hours	9	8.18
6-12hours	10	9.09
12-24hours	14	12.73
24-48hours	27	24.55
48-72hours	24	21.82
>72hours	26	23.64

The time for detection of hypoglycemia in newborn were 2-6 hours in 9 (8.18%), 6-12 hours in 10(9.09%), 12-24 hours in 14 (12.73%), 24-48 hours in 27 (24.55%), 48-72 hours in 24 (21.82%) and >72 hours in 26(23.64%) of cases.table 4.

In our study 80 (72.73%) neonates required oral feeds (EBM) for the correction of hypoglycemia, 28 (25.45%) required i.v. dextrose and 2 (1.82%) neonate required hydrocortisone.

Out of 110 neonates 9 (8.18%) neonates attained euglycemia within 30 minutes, 85(77.27%) in 1 hour, 11(10%) in 2 hours, 3 (2.73%) within 2-6 hours and 2 (1.82%) neonates required 6-12 hours to attain euglycemia. Out of 110 neonates 65 (59.09%) required 24 hours of hospital stay, 13 (11.82%) required 24-48 hours, 15(13.64%) required 48-72 hours, and 17(15.45%) required more than 72 hours of NICU stay.

In the present study 106 (96.36%) neonates recovered and mortality was observed in 4 (3.64%) neonates. All these neonates had become euglycemic following treatment but had expired because of the co-morbidities.

Discussion

In the present study among the 110 neonates with hypoglycemia, 66 (60%) were males and 54 (40%) were females. This was similar to the study conducted by Dhananjaya et al, Singh et al, Babu MR et al.[9-11].

The maternal risk factors that were associated with hypoglycemia were GDM, PIH, PROM. 18.18% had GDM, 10.90% had PIH and 1.82% had PROM as maternal risk factors. 68.18% had no maternal risk factor.

The percentage of GDM as a risk factor in hypoglycemic newborn (18.18%) in the present study was similar to that of Singhal et al (23.8%), because of the similar inclusion criteria for GDM[12]. 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.[11]PIH was a risk factor in study conducted by Singh et al (11%) which is

similar to the current study (11.67%)[10]. Percentage of PROM was very less (1.82%) when compared to other studies like Singh et al (8.5%), Amarendra et al (15.3%) as we took PROM more than 18 hours as a riskfactor[10,13].

In present study the neonatal risk factors associated with hypoglycemia were prematurity 21(28.18%), SGA 36(32.73%), LGA 7(6.36%), IDM 24(21.18%) and comorbidities (sepsis, birth asphyxia, polycythemia and shock) were present in 19(17.27%) of the hypoglycemic neonates. Among the comorbid condition birth asphyxia was present in 7 (6.64%), sepsis in 8(7.27%), polycythemia in 3(2.73%) and shock in 1 (0.91%). 82.73% 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%)[9,10,12]. SGA contributes 32.73% 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%)[10,12,14]. LGA contributes 6.36% of hypoglycemia in the present study which is similar to other studies by Singh et al (4.5%), Holtrope et al (5%)[10,15]. 19(17.27%) of the hypoglycemic neonates. Among the comorbid condition birth asphyxia was present in 7 (6.64%), sepsis in 8(7.27%), polycythemia in 3(2.73%) and shock in 1 (0.91%). 82.73% of the hypoglycemic neonates had at least one risk factor similar to the study conducted by Sashidaran et al (89.1%)[16].

Out of 110 children with hypoglycemia 74 (67.27%) were asymptomatic and 36 (32.73%) presented with symptoms. This was similar to the studies conducted by Singh et al, Singhal et al, Amerandra et al.[10,12,13]. The common symptoms were poor feeding (15.45%), lethargy (0.91%), jitteriness (3.64%), irritability (2.73%), hypotonia (0.91%) and cyanosis (0.91%). 30% of neonates presented with hypoglycemia on day 1 of life, 24.55% of neonates on day 2, 21.82% on day 3 and 23.64% 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[9]. The percentage of hypoglycemia in the study by Amarendra et al was very high in the first 24 hours (86.11%)[13]. In our study 80 (72.73%) neonates required oral feeds (EBM) for the correction of hypoglycemia, 28 (25.45%) required i.v. dextrose and 2 (1.82%) 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[10]. Out of 110 neonates 9 (8.18%) neonates attained euglycemia within 30 minutes, 85(77.27%) in 1 hour, 11(10%) in 2 hours, 3 (2.73%) within 2-6 hours and 2 (1.82%) neonates required 6-12 hours to attain euglycemia. Out of 110 neonates 65 (59.09%) required 24 hours of hospital stay, 13 (11.82%) required 24-48 hours, 15(13.64%) required 48-72 hours, and 17(15.45%) required more than 72 hours of NICU stay. In the present study 106 (96.36%) neonates recovered and mortality was in 4 (3.64%) neonates. similar to the studies done by Singh et al (90.2%).[10]Neonatal mortality was 3.64% 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. 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.

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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. Jane Hawdon. Metabolic disease: In: Janet M Rennie. Robertson's Textbook of Neonatology. 4th ed. Philadelphia: Elsevier; 2005. p.851-856.
2. Sperling MA. Hypoglycemia. In: Kliegman RM, Behrman RE, Jensen HB, Stanton BF, editors. Nelson Textbook of Pediatrics. 19th ed. Philadelphia, PA: Elsevier Inc.; 2012. p. 517-31.
3. Cornblath M, Schwartz R, Aynsley-Green A, Lloyd JK. Hypoglycemia in infancy: The need for a rational definition. A ciba foundation discussion meeting. Pediatrics 1990; 85:834-7.
4. Ghai OP. Ghai Essential Pediatrics: Newborn Infants. 8th ed. New Delhi: CBS Publication; 2013. p. 179-80.
5. Anysley GA, Soltesza G. Disorders of blood glucose homeostasis in the neonate. In: Robertson NR, editors. Textbook of Neonatology. London: Churchill Livingstone; 1986. p. 605-21.
6. Landon MB, Gabbe SG, Piana R, Mennuti MT, Main EK. Neonatal morbidity in pregnancy complicated by diabetes mellitus: Predictive value of maternal glycemic profiles. Am J Obstet Gynecol 1987; 156:1089-95.
7. Saudubray JM, Narcy C, Lyonnet L, Bonnefont JP, Poll The BT, Munnich A, *et al*. Clinical approach to inherited metabolic disorders in neonates. Biol Neonate 1990;58 Suppl 1:44-53.
8. Dean AG, Sullivan KM, Soe MM. Open Epi: Open-Source Epidemiologic Statistics for Public Health, Version 3.01. Availabl from: https://www.openepi.com/Menu/OE_Menu.htm. Accessed on 16 August 2018.
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.2019;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.2019;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).