DOI: https://doi.org/10.53350/pjmhs2115123962

ORIGINAL ARTICLE

Frequency of Hypoglycemia in Preterm Newborns

IBRAHIM[1], FAIQA HASSAN[2], MUHAMMAD SHAHID GHAFFAR[3], ADNAN BASHIR[4], TAHIR MAHMOOD[5], ABID RAFIQ CHAUDHRY[6]

[1]Assistant Professor Peads Medicine, Swat Medical College / Swat Medical Complex Teaching Hospital, Saidu Sharif Swat and Children Medical Centre(CMC) / Dr Habib un Nabi Children Hospital, Airport Road Mingora Swat
[2]Senior Registrar Pediatrics, Memon Medical Institute, Karachi
[3]Assistant Professor of Paediatric, Hamdard University Hospital, Karachi
[4]Assistant Professor Paediatrics, Hamdard College of Medicine and Dentistry, Karachi
[5]Associate Professor of Pediatrics, Pediatric department FMU /Allied hospital, Faisalabad
[6]Consultant Pediatrics, Fatima Memorial Hospital, Lahore
Corresponding author: Ibrahim, Email: dribrahimsr@gmail.com, Cell: 03459526432

ABSTRACT

Objective: The purpose of this study is to determine the prevalence of hypoglycemia and its increased risk of morbidity and mortality in preterm newborns.

Study Design: Cross-sectional

Place and Duration: Study was conducted at Children Medical Center (CMC) / Dr Habib un Nabi Children Hospital Airport Road Mingora Swat and Memon Medical Institute Karachi for duration of six months from January 2021 to June 2021.

Methods: Total 120 preterm neonates had symptomatic and asymptomatic hypoglycemia was presented in this study. Detailed demographics included sex, birth weight and gestational age were recorded after taking informed written consent from the authorities. Blood sample was taken from all neonates for laboratory test. Blood glucose <40mg/dl were calculated as hypoglycemia. Frequency of hypoglycemia and its risk factors with symptoms were calculated in this study. SPSS 22.0 version was used to analyze all data.

Results: Majority of the infants were males 75 (62.5%) and 45 (37.5%) were females. Mean gestational age was 32.3+6.37 weeks. Mean birth weight of the infants was 2.04±3.43 kg with mean age 4.5+3.73 days. Out of 120 cases, 88 (73.3%) neonates were born by C-section. Frequency of hypoglycemia was fund among 52 (43.3%) cases in which majority were males with symptomatic hypoglycemia in 40 (33.3%) neonates. Hypertension in mothers was the most common cause of hypoglycemia found in 27 (51.9%) cases. Breast feeding difficulty was the most common symptom in 43 (82.7%) cases followed by jitteriness in 32 (61.5%). Rate of mortality was 7 (13.5%).

Conclusion: In this research we concluded that the prevalence of hypoglycemia was significantly higher in preterm neonates and maximum cases were reported in symptomatic neonates with higher number of males. For children, hypoglycemia is associated with a high mortality risk. If a child's blood sugar levels go dangerously low or if they've been fasting for an extended period of time, they should receive treatment.

Keywords: Preterm Newborns, Hypoglycemia, Prevalence, Mortality, Symptoms

INTRODUCTION

Late in the 19th century, Harris invented the term "hypoglycemia," which refers to a drop in blood sugar levels. Harris first used the term to describe his own experience with hypoglycemia. [1] Low blood glucose, especially for neonates, has been studied extensively in recent decades, however there is no consensus about what constitute a low blood glucose level and what is an appropriate level for different neonates. Clinical signs and test values for hypoglycemia have subsequently been described and the therapy to this problem has been adapted to each infant's specific physiologic adaptations. As early as 1937, a link was established between hypoglycemia and brain abnormalities in premature newborns. Because of this, low blood sugar levels were divided into three categories: "mild," "moderate," and "severe," with "severe" being defined as 20 mg/dL (1.1 mmol/L) or higher. [2] One group of researchers proposed a normal low glucose range of 30–35 mg/dL (1.67–1.94 mmol/L) during the first 24 hours of life; 45 mg/dL (2.5 mmol/L) following feeding and 40–50 mg/dL (2.22–2.78 mmol/L) after the completion of the first 24 hours of life. [3] There have since been a number of operational thresholds defined. Neonatal glucose levels have been debated by both the American Academy of Pediatrics and the Pediatric Endocrine Society (PES). According to current research, plasma glucose levels drop to 1.67 millimoles per litre in the first two hours of life, then climb to at least 45 millimoles per litre (2.5 mmol/L) before stabilising between 12 and 24 hours after birth. Hypoglycemia in neonates is defined by the AAP by using a numerical plasma glucose measurement of 47 mg/dL (2.6 mmol/L). [4] [5]

In spite of the fact that hypoglycemia is associated with a lower blood glucose level, its numerical definition has been the subject of much debate and confusion in the medical community.[6] Clinical indications of hypoglycemia may not be apparent in newborns since their brains are still developing. Insufficient studies have been undertaken to develop a consensus on the lowest tolerable glucose level for asymptomatic hypoglycemia.[7] To help prevent hypoglycemia in infants, the American Academy of Pediatrics' Committee on Fetus and Newborn (CFN) established acceptable glucose concentrations in its 2011 guidelines. Cornblath and Ichord's[8] guidelines in 2000 were used to determine the glucose levels in babies requiring intervention in the guide. First 24 hours were divided into two halves, and operational threshold values were established accordingly based on metabolic

adaption.Pregnancy begins to collect glycogen at at 27 weeks gestation, with a gradual increase until 36 weeks gestation, then a rapid accumulation to reach 50 mg/g of tissue by term. glucose concentration drops to 3–3.3 mmol/L in term newborns in the first 1–2 hours after birth.[9]

Preterm newborns rely on glycogen stored in their bodies to maintain their own glucose levels. Due to their smaller glycogen stores, preterm babies are more susceptible to hypoglycemia after birth. [10] Additionally, they may be subjected to increased prenatal stress, which may result in premature birth. When it comes to the incidence and possible risk factors for hypoglycemia in premature newborns, there is a paucity of research to support this claim. When a newborn is born late preterm or term, the risk of neonatal hypoglycemia increases if the mother is diabetic, the baby is born SGA or LGA, or if the mother has high blood pressure. [11,12]

An investigation into the prevalence of hypoglycemia in symptomatic/asymptomatic neonates was the primary objective of this study. Morbidity can be reduced in both the short- and long-term by detecting hypoglycemia at an early stage.

MATERIAL AND METHODS

This cross-sectional study was conducted at Children Medical Center (CMC) / Dr Habib un Nabi Children Hospital Airport Road Mingora Swat and Memon Medical Institute Karachi for duration of six months from January 2021 to June 2021. The study was comprised of 120 preterm neonates. Detailed demographics included sex, birth weight and gestational age were recorded after taking informed written consent from the authorities. There was no consideration given to newborns with gross dysmorphism or those who presented after 7 days of delivery without confirmation of gestational age or birth weight.

Hypoglycemia symptoms in singleton neonates, such as seizures, jitteriness, lethargy and refusal to feed as well as respiratory distress and hypotonia (as well as hypothermia and aberrant crying) were reported within seven days of birth. Peripheral vein blood was drawn and delivered to the lab for testing of blood glucose, total serum calcium, serum electrolytes (Na, K), and complete blood count using aseptic technique. Clinical suspicion led to the collection of additional specimens, including blood cultures and cerebrospinal fluid. Additional testing included a chest x-ray and an echocardiogram on chosen newborns. Hypoglycemia was defined as a blood glucose level of less than 40 mg/dl (2.2mmol/l). Neonatal hypoglycemic patients were given glucose intravenously (I.V.) in accordance with accepted practices7. Hypoglycemic babies had their blood glucose levels checked every six hours. I.V. glucose was administered to hypoglycemic infants with clinical suspicions of birth asphyxia and/or neonatal infection. Symptoms of hypoglycemia were ruled out if glucose levels rose. Asphyxia and/or newborn sepsis were blamed for symptoms that persisted even after blood glucose levels were brought back to normal.

Frequency of hypoglycemia and its risk factors with symptoms were calculated in this study. SPSS 22.0 version was used to analyze all data. Mean standard deviation, frequency and percentages were used for categorical variables.

RESULTS

Majority of the infants were males 75 (62.5%) and 45 (37.5%) were females. Mean gestational age was 32.3+6.37 weeks. Mean birth weight of the infants was 2.04±3.43 kg with mean age 4.5+3.73 days. Out of 120 cases, 88 (73.3%) neonates were born by C-section and remaining was by normal delivery.(table 1)

Table 1: Baseline characteristic of enrolled cases

Variables	Frequency	Percentage
Gender		
Male	75	62.5
Female	45	37.5
Mean age (Days)	4.5±3.73	
Gestational age (weeks)	32.3±6.37	
Mean birth weight (kg)	2.04±3.43	
Delivery		
C-section	88	73.3
Normal	32	26.7

Frequency of hypoglycemia was fund among 52 (43.3%) cases in which majority were males with symptomatic hypoglycemia in 40 (33.3%) neonates.(table 2)

Table 2: Prevalence of hypoglycemia among enrolled babies

Variables	Frequency (120)	Percentage
Hypoglycemia		
Yes	52	43.3
No	68	56.7
Types		
symptomatic	40	33.3
asymptomatic	12	10
Gender		
Male	32	61.5
Female	20	38.5

Hypertension in mothers was the most common cause of hypoglycemia found in 27 (51.9%) cases.(table 3)

Table 3: Causes of hypoglycemia among infants

Variables	Frequency (52)	Percentage
Hypertension	27	51.9
Medication	12	23.1
Alcohol	9	17.3
Severe Illness	4	7.7

Breast feeding difficulty was the most common symptom in 43 (82.7%) cases followed by jitteriness in 32 (61.5%). (table 4)

Table 4: Association of symptoms among cases for hypoglycemia

Variables	Frequency (44)	Percentage
Symptoms		
difficulty in feeding	43	82.7
jitteriness	32	61.5
seizures	21	40.4
Respiratory distress	19	36.5
hypothermia	13	25

Rate of mortality was 7 (13.5%) among 44 cases of hypoglycemia.(table 5)

Table 5: Frequency of death among neonates

Variables	Frequency (44)	Percentage
Mortality		
Yes	7	13.5
No	45	86.5

DISCUSSION

Neonatal hypoglycemia continues to be a common issue. Neonatal hypoglycemia has been the subject of much research because of the link between low blood glucose levels and aberrant development. Local, regional, and worldwide research have been done yet there are still many unanswered questions, particularly in poor countries. Hyperglycemia has gotten far less attention than hypoglycemia, which is a well-known sign of newborn sepsis. Hyperglycemia was recorded in 24.6 percent of NICU admissions, with sepsis accounting for 78.8 percent of cases; however, no data was provided on how common hyperglycemia was among sepsis patients. [13]

In this cross-sectional study 120 preterm neonates were presented. Majority of the infants were males 75 (62.5%) and 45 (37.5%) were females. Mean gestational age was 32.3+6.37 weeks. Mean birth weight of the infants was 2.04±3.43 kg with mean age 4.5+3.73 days. Findings of current study were comparable to the studies conducted in past.[14,15] Hypertension in mothers was the most common cause of hypoglycemia found in 27 (51.9%) cases. Hypoglycemia was three and a half times as likely in women with maternal hypertension than in those without it. Neonate hypoglycemia has been linked to maternal hypertension in the past. It can also be an indication of other problems, including preterm, SGA, or a lack of placenta adequacy throughout pregnancy. [16] Neonatal hypoglycemia is associated with maternal beta blocker use as well. [17]

Out of 120 cases, 88 (73.3%) neonates were born by C-section. Frequency of hypoglycemia was fund among 52 (43.3%) cases in which majority were males with symptomatic hypoglycemia in 40 (33.3%) neonates. Our study found that neonatal hypoglycemia is a common occurrence, particularly in those with signs and symptoms. Hypoglycemia is more common in our population because of causes such as preterm births, intrauterine growth retardation, sepsis, and perinatal asphyxia, which are more common in our population.[19] The risk of newborn hypoglycemia in late preterm infants born at 34–36 weeks of gestation has been linked to antenatal steroid treatment. [20] In infants 32 weeks gestation, James-Todd et al. reported an overall incidence of 41%, however they employed point of care glucose levels that have poor sensitivity in the hypoglycemic range and excluded infants of diabetes mothers. [21] A 51 percent incidence was observed in children under 35 weeks of gestation within the first 48 hours of their lives by Harris et al in their study. [22] A recent study found that the nadir of plasma glucose concentration in preterm newborns and extremely preterm infants is at 70.5 and 60.9 minutes, respectively. [23]

Breast feeding difficulty was the most common symptom in 43 (82.7%) cases followed by jitteriness in 32 (61.5%).[24] Burdan DR et al also identified more preterm babies as hypoglycemia than term babies (52.8 percent Vs 45.53 percent). (52.8 percent Vs 45.53 percent). Hypoglycemia was seen in 8.3 percent large for gestational age neonates in our trials. These findings are congruent with those of Burdan DR et al. [25] The risk of newborn hypoglycemia is raised in infants born SGA because of a lack of glycogen and fat stores, an incorrect release of insulin, and a lack of counter-regulatory hormones. [26] This extra development and inability to respond to hypoglycemia prenatally is caused by greater hyperinsulinism in infants born LGA. [27]

Rate of mortality was 7 (13.5%) among 44 cases of hypoglycemia. It was previously found that nine of those 21 deaths (42.8 percent) happened within 24 hours of admission and five (1.4 percent) occurred within three days after discharge when a systematic call to parents was made. According to our earlier research in Madagascar and Mali, the early death rate could reach as high as 50% and 87%, respectively. In tropical paediatric institutions, this is a regular occurrence due to the high number of children who arrive with severe and advanced sickness. At the unit level, the availability of quick diagnostic tools, the availability of emergency drugs, and the ability to initiate resuscitation must be increased [29,30].

Hypoglycemia is prevalent in newborns, particularly in the first week. Male babies are more likely to suffer from this condition. There should be mandatory blood glucose screenings for infants with signs and symptoms. A high suspicion of hypoglycemia is recommended for early detection, timely treatment, and a better outcome based on our results.

CONCLUSION

In this research we concluded that the prevalence of hypoglycemia was significantly higher in preterm neonates and maximum cases were reported in symptomatic neonates with higher number of males. For children, hypoglycemia is associated with a high mortality risk. If a child's blood sugar levels go dangerously low or if they've been fasting for an extended period of time, they should receive treatment.

REFERENCE

1 Harris S. Hyperinsulinism and dysinsulinism. JAMA 1924;83:729-33. 10.1001/jama.1924.02660100003002

2 Hypoglycemia Hartmann A. J Pediatr 1998;132:1-3. 10.1016/S0022-3476(98)70474-3 [

3 Cornblath M, Ichord R. Hypoglycemia in the neonate. Semin Perinatol 2000;24:136-49. 10.1053/sp.2000.6364

4 Heck LJ, Erenberg A. Serum glucose levels in term neonates during the first 48 hours of life. J Pediatr 1987;110:119-22. 10.1016/S0022-3476(87)80303-7

5 Committee on Fetus and Newborn , Adamkin DH. Postnatal glucose homeostasis in late-preterm and term infants. Pediatrics 2011;127:575-9. 10.1542/peds.2010-3851

6 N. Boluyt, A. van Kempen, M. Offringa.Neurodevelopment after neonatal hypoglycemia: a systematic review and design of an optimal future study. Pediatrics, 117 (2006), pp. 2231-2243

7 Committee on Fetus and Newborn, D.H. Adamkin.Postnatal glucose homeostasis in late-preterm and term infants.Pediatrics, 127 (2011), pp. 575-579

8 M. Cornblath, R. Ichord. Hypoglycemia in the neonate.Semin Perinatol, 24 (2000), pp. 136-149

9 Mitanchez D. Glucose regulation in preterm newborn infants. Horm Res. (2007) 68:265–71.

10 Stanley CA, Rozance PJ, Thornton PS, De Leon DD, Harris D, Haymond MW, et al. Re-evaluating transitional neonatal hypoglycemia: mechanism and implications for management. J Pediatr. (2015) 166:1520–25.

11 Adamkin DH Committee on fetus and newborn. postnatal glucose homeostasis in late-preterm and term infants. Pediatrics. (2011) 127:575–9.

12 Thornton PS, Stanley CA, De Leon DD, Harris D, Haymond MW, Hussain K, et al. Recommendations from the pediatric endocrine society for evaluation and management of persistent hypoglycemia in neonates, infants, and children. J Pediatr. (2015) 167:238–45

13 Mohammed MM, Abdel Rahman SM (2016) Frequency of neonatal hyperglycaemia at Gaafar Ibnauf Children's Hospital: clinical aspects and short term outcome. Sudan J Paediatr 16(1):45–52

14 Sharma A, Davis A, Shekhawat PS. Hypoglycemia in the preterm neonate: etiopathogenesis, diagnosis, management and long-term outcomes. Transl Pediatr. 2017;6(4):335-348.

15 Mitchell NA, Grimbly C, Rosolowsky ET, O'Reilly M, Yaskina M, Cheung P-Y and Schmölzer GM (2020) Incidence and Risk Factors for Hypoglycemia During Fetal-to-Neonatal Transition in Premature Infants. Front. Pediatr. 8:34. doi: 10.3389/fped.2020.00034

16 Bateman BT, Patorno E, Desai RJ, Seely EW, Mogun H, Maeda A, et al. Late pregnancy ß blocker exposure and risks of neonatal hypoglycemia and bradycardia. Pediatrics. (2016) 138:e20160731.

17 Chollat C, Sentilhes L, Marret S. Protection of brain development by antenatal magnesium sulphate for infants born preterm. Dev Med Child Neurol. (2018) 61:25–30.

18 Nihan Hilal Hosagasi, Mustafa Aydin, Aysegul Zenciroglu, Nuran Ustun, Serdar Beken,

19 Incidence of hypoglycemia in newborns at risk and an audit of the 2011 American academy of pediatrics guideline for hypoglycemia,Pediatrics & Neonatology, Volume 59, Issue 4, 2018, Pages 368-374, ISSN 1875-9572,

20 Gyamfi-Bannerman C, Thom EA, Blackwell SC, Tita AT, Reddy UM, Saade GR, et al. Antenatal betamethasone for women at risk for late preterm delivery. N Engl J Med. (2016) 374:1311–20.

21 James-Todd T, March MI, Seiglie J, Gupta M, Brown FM, Majzoub JA. Racial differences in neonatal hypoglycemia among very early preterm births. J Perinatol. (2018) 38:258–63.

22 Harris DL, Weston PJ, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. J Pediatr. (2012) 161:787–91.

23 Kaiser JR, Bai S, Rozance PJ. Newborn plasma glucose concentration nadirs by gestational-age group. Neonatology. (2018) 113:353–59.

24 Dashti N, Einollahi N, Abbasi S. Neonatal hypoglycemia: prevalence and clinical manifestations in Tehran Children's Hospital. Pak J Med Sci 2007; 23: 340-3

25 Burdan DR, Botiu V, Teodorescu D. Neonatal hypoglycemia. The incidence of the risk factors in Salvator VUIA Obstetrics-Gynecology Hospital, ARAD.TMJ 2009; 59:77-80

26 Avci ME, Sanlikan F, Celik M, Avci A, Kocaer M, Göçmen A. Effects of maternal obesity on antenatal, perinatal and neonatal outcomes. J Matern Fetal Neonatal Med. (2015) 28:2080–83

27 Güemes M, Hussain K. Hyperinsulinemic hypoglycemia. Pediatr Clin North Am. (2015) 62:1017–28. Sambany E, Pussard E, Rajaonarivo C, Raobijaona H, Barennes H. (2013) Childhood dysglycemia: prevalence and outcome in a referral hospital. PLoS One 8: e65193. PONE-D-11-12466 [pii]. pmid:23741481

29 Willcox ML, Forster M, Dicko MI, Graz B, Mayon-White R, Barennes H. (2010) Blood glucose and prognosis in children with presumed severe malaria: is there a threshold for 'hypoglycaemia'? Trop Med Int Health 15: 232–240.

30 Fernández Martínez MDM, Llorente JLG, de Cabo JM, López MAV, Porcel MDCO, Rubio JDD, Perales AB. Monitoring the Frequency and Duration of Hypoglycemia in Preterm Infants and Identifying Associated Factors. Fetal Pediatr Pathol. 2021 Apr;40(2):131-141