Journal of Acute Disease

Short Communication

jadweb.org

doi: 10.4103/jad.jad_109_23 Impact Factor® 0.5

Clinical profile and risk factors of symptomatic and asymptomatic hypoglycemia in neonates admitted to NICU in a tertiary care center: A cross-sectional study

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ABSTRACT

Objective: To investigate the clinical profile and risk factors of symptomatic and asymptomatic hypoglycemia in neonates admitted to a neonatal intensive care unit in a tertiary care center.

Methods: The prospective observational study was conducted in a tertiary care center in the Specialty Department of Pediatric. 196 Newborn babies with blood glucose levels < 45 mg/dL were examined with a simple random sampling method between December 2019 and November 2021. Maternal and neonatal risk factors and clinical signs were recorded and compared between symptomatic and asymptomatic cases.

Results: The proportion of symptomatic hypoglycemia neonates born to gestational diabetes mellitus mothers was significantly higher (23.4% *vs.* 8.4%)(P<0.05). Small for gestational age, low birth weight, respiratory distress syndrome, hypothermia, and endocrine disorders were risk factors. The death rate in asymptomatic hypoglycemia neonates was significantly higher (58% *vs.* 39%) (P<0.05).

Conclusions: The study indicates that maternal gestational diabetes mellitus is associated with symptomatic hypoglycemia and asymptomatic hypoglycemia is associated with neonatal mortality. It is important to take vigilance and timely interventions to address associated symptoms, particularly poor feeding, in the management of neonatal hypoglycemia.

KEYWORDS: Hypoglycemia; Neonatal diabetes; Symptomatic; Asymptomatic; Newborns hypoglycemia; Diabetic infants; Prevalence

1. Introduction

In neonates, hypoglycemia is the most prevalent but preventable metabolic disorder that can cause brain damage, mental retardation, and even death. Long-term hypoglycemia in newborns can lead to irreversible brain damage and may lead to seizures, recurrent seizures, and personality disorders.

Atrophic gyri, decreased myelination, and atrophy of cerebral

Significance

Neonatal hypoglycemia, a significant risk for newborns, poses challenges in detection due to diverse presentations and diagnostic uncertainties. Our study revealed a high prevalence of asymptomatic (60.7%) and symptomatic (39.3%) hypoglycemia in newborns. Maternal gestational diabetes, small for gestational age, low birth weight, respiratory distress syndrome, hypothermia, and endocrine disorders are risk factors. These findings could enhance screening, interventions, and care protocols, potentially mitigating long-term neurological complications and mortality in at-risk neonates.

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How to cite this article: Bhaisare KB, Mundada SK, Shah NB. Clinical profile and risk factors of symptomatic and asymptomatic hypoglycemia in neonates admitted to NICU in a tertiary care center: A cross-sectional study. J Acute Dis 2024; 13(1): 31-35.

Article history: Received 14 November 2023; Revision 20 December 2023; Accepted 17 January 2024; Available online 28 February 2024

white matter are all symptoms of the pathogenic alterations[1]. Blood glucose is essential for normal neurological growth and function. Preterm and small for gestational age (SGA) newborns are predisposed to prolonged hypoglycemia due to a lack of liver glycogen and fat reserves and an undeveloped metabolic pathway at delivery[1-3]. Hyperinsulinemia and hypoglycemia are common in infants of diabetic mothers. Islet cell dysregulation syndrome (nesidioblastosis), Beckwith-Wiedemann syndrome, insulin-secreting adenoma, congenital hypopituitarism, glycogen storage diseases and defects of amino acid metabolism are all known causes. Due to the lack of a strong association between plasma glucose levels, clinical symptoms, and long-term consequences, the diagnosis of hypoglycemia in newborns has remained a point of contention[4]. Hypoglycemia is characterized as a glucose level that is two standard deviations below the population mean. Serum glucose levels in healthy-term neonates are rarely less than 35 mg/dL between 1 and 3 hours of life, 40 mg/dL between 3 and 24 hours, and 45 mg/dL after 24 hours[5,6]. The incidence of hypoglycemia varies depending on the definition, population, feeding method and timing, as well as the type of glucose assay used. Overall, incidences range from 1 to 5 per 1 000 live births, with up to 16% of large-for-gestational-age (LGA) neonates, 15% of SGA neonates, and 5%-10% of preterm neonates being affected[5-7].

In healthy full-term neonates, hormonal and metabolic adaptations ensure an adequate energy substrate for the vital organs during the immediate neonatal period after birth. However, this hormonal-metabolic adaptation after birth fails to varying degrees in preterm and SGA infants. As a result, hypoglycemia is more likely in the first 72 hours of birth. The overall rate of newborn hypoglycemia is 1 to 5 per 1 000 live births, with rates as high as 30% in high-risk neonates. Rates vary by region. The incidence is 15% in preterm and intrauterine development-delayed neonates and 8% in LGA infants, especially in diabetic mothers' babies[8].

Symptoms range from lethargy, jitteriness, apnea, irritability, and seizures to complete asymptomatic hypoglycemia. Treatment options depend on the birth weight and gestational age of the baby.

Intravenous glucose is frequently required if blood glucose levels remain low in newborns. Breastfeeding is the first line of defense against asymptomatic hypoglycemia. Newborns who were exclusively breastfed had lower blood glucose levels than those who were fed formula.

Neonatal hypoglycemia is a topic that needs to be reevaluated because the relationship between plasma glucose concentration, clinical symptoms, and long-term consequences is poorly understood, there are disagreements about the best way to detect it and neonatal hypoglycemia continues to occur despite increased institutional deliveries and advances in neonatal care practices.

As a result, the current study was undertaken to investigate the clinical profile and risk factors for symptomatic and asymptomatic hypoglycemia in newborns in the neonatal intensive care unit (NICU), as well as to compare the clinical profile and risk factors in two groups of neonates.

2. Patients and methods

This cross-sectional study was conducted in the NICU of a tertiary care center specializing in the Department of Pediatrics from December 2019 to November 2021.

2.1. Inclusion and exclusion criteria

Newborns with a blood glucose level <45 mg/dL of both sexes were included. Neonates with blood glucose levels >45 mg/dL and those with congenital anomalies or breastfeeding problems (*e.g.*, cleft lip and palate) were excluded.

2.2. Data collection

The study investigated symptomatic outcomes including gestational diabetes mellitus (GDM), and highlighted an association between asymptomatic hypoglycemia and higher neonatal mortality rates. It examined various maternal risk factors such as pregnancy-induced hypertension (PIH) and premature rupture of membranes (PROM), as well as neonatal risk factors including prematurity, SGA, LGA, low birth weight (LBW), mortality rates, and laboratory parameters.

2.3. Statistical analysis

IBM's SPSS 24.0 edition was used. Data were expressed as frequency and percentages. Chi-square test was used for analysis of qualitative variables. In all analyses, statistical significance was set at $P<0.05$.

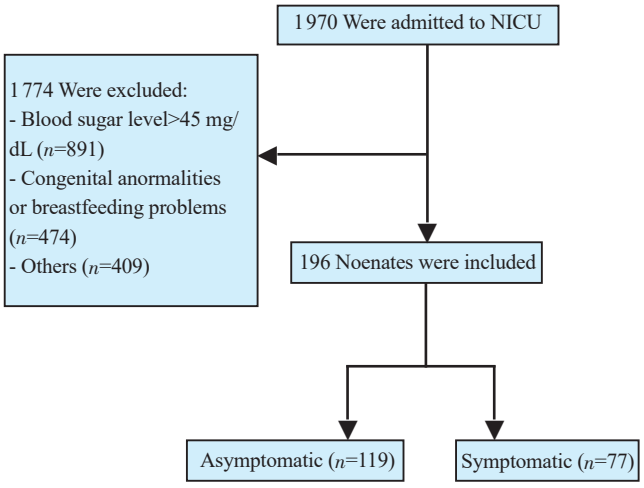

Figure 1. The study flowchart.

Table 1. Basic characteristics (n=196, n, %).

Variables	Asymptomatic (n=119)	Symptomatic (n=77)
Mothers´ age (years)		
21-25	98 (82.4)	64 (93.1)
26-30	21 (17.6)	13 (16.9)
Time (hours)		
<24	36 (30.3)	19 (24.7)
25-48	13 (10.9)	13 (16.7)
49-72	12 (10.1)	8 (10.4)
>72	58 (48.7)	37 (48.1)
Parity		
Multipara	57 (47.9)	33 (42.9)
Primipara	62 (52.1)	44 (57.1)
Mode of delivery		
LSCS	64 (53.8)	43 (55.8)
NVD	55 (46.2)	34 (44.2)
Maturity		
Preterm	86 (72.3)	32 (41.6)
Term	33 (27.7)	45 (58.4)
Gestational age		
AGA	28 (23.5)	34 (44.2)
LGA	2 (1.7)	10 (13.0)
SGA	89 (74.8)	33 (42.9)

LSCS: Lower segment caesarian section; NVD: Normal vaginal delivery; AGA: Appropriate for gestational age; LGA: Large for gestational age; SGA: Small for gestational age.

3. Results

In the present study, the total number of admissions in NICU was 1970 during the study period, out of which 196 were hypoglycemic (9.94%). 196 Neonates were included. 119 Had asymptomatic (60.7%) and 77 had symptomatic hypoglycemia (Figure 1).

3.1. Basic characteristics

Most mothers were between the ages of 21-25 years old in both two groups. Most cases occurred with the time of onset of >72 hours. More hypoglycemia newborns were born *via* primipara and lower segment caesarian section. Preterm and SGA newborns had higher incidences of asymptomatic hypoglycemia; while term and appropriate for gestational age (AGA) newborns had higher incidences of symptomatic hypoglycemia (Table 1).

Table 2. Association of hypoglycemia with maternal risk factors (n=196, n, %).

Variables	Asymptomatic (n=119)	Symptomatic (n=77)	χ^2	*P*
GDM				
Yes	10 (8.4)	18 (23.4)	8.55	<0.01
No	109 (91.6)	59 (76.6)		
PIH				
Yes	15 (12.6)	8 (10.4)	0.22	0.63
No	104 (87.4)	69 (89.6)		
PROM				
Yes	1 (0.8)	3 (3.9)	2.18	0.13
No	118 (99.2)	74 (96.1)		
Use of OHA				
Yes	8 (6.7)	7 (9.1)	0.37	0.54
No	111 (93.3)	70 (90.9)		
Metabolic diseases				
Yes	10 (8.4)	7 (9.1)	0.02	0.86
No	109 (91.6)	70 (90.9)		

GDM: gestational diabetes mellitus; PIH: pregnancy-induced hypertension; PROM: premature rupture of membrane; OHA: oral hypoglycemic agents.

Table 3. Association of hypoglycemia with neonatal risk factors (n=196, n, %).

Variables	Asymptomatic (n=119)	Symptomatic (n=77)	χ^2	*P*
Prematurity				
Yes	34 (28.6)	19 (24.7)	0.35	0.54
No	85 (71.4)	58 (75.4)		
SGA				
Yes	42 (35.3)	15 (19.5)	5.66	<0.05
No	77 (64.7)	62 (80.5)		
LBW				
Yes	72 (60.5)	22 (28.6)	19.10	<0.01
No	47 (39.5)	55 (71.4)		
RDS				
Yes	43 (36.1)	17 (22.1)	4.34	<0.01
No	76 (63.9)	60 (77.9)		
Birth asphyxia				
Yes	6 (5.0)	8 (10.4)	2.01	0.15
No	113 (95.0)	69 (89.6)		
Sepsis				
Yes	27 (22.7)	12 (15.6)	1.48	0.22
No	92 (77.3)	65 (84.4)		
Hypothermia				
Yes	30 (25.2)	19 (24.7)	0.01	0.93
No	89 (74.8)	58 (75.3)		
Endocrine disorder				
Yes	0 (0.0)	7 (9.1)	11.21	<0.01
No	119 (100)	70 (90.6)		
Inborn error of metabolism				
Yes	5 (4.2)	2 (2.6)	0.34	0.55
No	114 (95.8)	75 (97.6)		
Inadequate feeding				
Yes	37 (31.1)	32 (41.6)	2.24	0.13
No	82 (68.9)	45 (58.4)		

3.2. Maternal risk factors

The proportion of asymptomatic hypoglycemia neonates born to GDM mothers was 8.4% compared to 23.4% of symptomatic hypoglycemia neonates born to GDM mothers, with a statistically significant difference between the two groups (P<0.05), indicating that maternal GDM is associated with symptomatic hypoglycemia (Table 2). There was no significant difference in incidence of PIH, PROM, metabolic diseases, or use of oral hypoglycemic agents between the two groups (P>0.05).

3.3. Neonatal risk factors

Table 3 shows that SGA, LBW, RDS, hypothermia, and endocrine disorders were risk factors. The incidences of SGA, LBW, RDS, and hypothermia in the symptomatic hypoglycemia were lower and incidence of endocrine disorders was higher (P<0.05).

3.4. Mortality in symptomatic and asymptomatic hypoglycemia neonates

The death rate in asymptomatic hypoglycemia neonates was 58%, compared to 39% in symptomatic hypoglycemia neonates, with a statistically significant difference between the two groups (P<0.05), indicating that asymptomatic hypoglycemia is associated with neonatal mortality in our study.

3.5. Association of laboratory parameters with hypoglycemia

CRP was positive in 26 asymptomatic hypoglycemia cases (21.8%) and 13 symptomatic hypoglycemia cases (16.9%). Platelets were reduced in 21.8% of asymptomatic hypoglycemia cases and 16.9 symptomatic hypoglycemia cases. WBC was increased in 21.8% of asymptomatic hypoglycemia cases and 16.9% of symptomatic hypoglycemia cases. Serum electrolyte and neurosonogram were normal in all the asymptomatic and symptomatic cases. All differences were not significant (P>0.05).

4. Discussion

In our study, out of 1970 neonates, 196 (9.94%) were diagnosed with hypoglycemia. The findings from Manjunatha Babu *et al*.'s study exhibit similar results[9], with an incidence of 8.26%, slightly lower than our study. While the prevalence of neonatal hypoglycemia reported by Somanathan *et al*. was 14.9% among NICU admissions[10].

The study compared maternal risk factors such as GDM, PIH, and PROM, neonatal risk factors such as prematurity, SGA, LGA, and clinical signs between symptomatic and asymptomatic cases. The results showed significant differences in case numbers of AGA, LGA, and SGA babies between symptomatic and asymptomatic hypoglycemia cases. Maternal GDM is significantly associated with hypoglycemia incidence. The findings from the study by Madavi *et al*. show a higher prevalence of hypoglycemia among male neonates and also highlight neonatal risk factors like RDS and septicemia as well as maternal risk factors such as PIH and PROM[11].

This study still has several limitations. It is retrospective and might result in potential selection bias or incomplete data capture. Generalizability might be limited due to the study being conducted in a specific tertiary care center. The study's sample size might not represent the broader neonatal population. A lack of detailed information on certain maternal and neonatal factors or potential confounders might affect the study's accuracy. Variability in clinical presentation and diagnostic criteria for hypoglycemia across different settings might impact the interpretation of results.

In conclusion, we found that 60.7% of newborns had asymptomatic hypoglycemia and 39.3% had symptomatic hypoglycemia, with a strong link between maternal GDM and symptomatic hypoglycemia, and a strong link between hypoglycemia and SGA, LBW, RDS, hypothermia, and endocrine disorders.

Conflict of interest statement

The authors report no conflict of interest.

Funding

This study received no extramural funding.

Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Authors' contributions

KB conceived of the study. KB and SM reviewed the literature, conducted the quality assessment, and extracted the data. KB developed the methods, supported the data interpretation, and drafted the manuscript. NS reviewed and collected the data. KB was the project manager and advisor on the project. All authors read and approved the final manuscript.

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Edited by Tan BJ, Chen SR