Section: Pediatrics

Original Research Article

A STUDY OF NEONATAL HYPOGLYCAEMIA AND ITS CORRELATION WITH LOW-BIRTH-WEIGHT NEONATES

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ABSTRACT

Background: Aims: Neonatal hypoglycaemia, a common metabolic disorder, is particularly prevalent among low birth weight (LBW) neonates, contributing to significant morbidity and mortality. Despite its clinical significance, no universal consensus exists on optimal screening and management protocols. This study aimed to examine the association between neonatal hypoglycaemia and LBW, focusing on prevalence, risk factors, and clinical implications to refine management strategies and improve neonatal outcomes.

Materials and Methods: This prospective longitudinal study was conducted in the Paediatric Newborn Unit of T.S. MISRA Medical College and Hospital, Lucknow, over 18 months. Fifty-eight LBW neonates (<2500 g) were enrolled. Blood glucose levels were measured at specific intervals, and neonates with blood glucose ≤40 mg/dL were classified as hypoglycaemic. Statistical analysis was performed using SPSS 25.0, with a p-value <0.05 considered significant.

Results: The incidence of hypoglycaemia was 25.8%. Hypoglycaemic neonates were predominantly preterm (80%) and small-for-gestational-age (60%), both showing significant associations ($p<0.05$). Birth asphyxia (53.3%) was a major risk factor ($p=0.017$), while maternal factors, including pre-eclampsia and PROM, were not significantly associated. Multivariate logistic regression highlighted gestational age as the strongest predictor (OR = 7.943, $p<0.001$).

Conclusion: Preterm and SGA neonates are at heightened risk for hypoglycaemia, emphasizing the need for targeted glucose monitoring and early intervention. While maternal factors were less significant, neonatal factors such as birth weight and asphyxia played critical roles. The study underscores the importance of proactive management to mitigate complications and improve neonatal outcomes.

Keywords: Neonatal hypoglycaemia, Low birth weight, Preterm neonates, Small-for-gestational-age, Neonatal outcomes.

INTRODUCTION

Neonatal hypoglycaemia is a common metabolic disorder, particularly in low birth weight (LBW) neonates, who face a higher risk of morbidity and mortality. The World Health Organization (WHO) defines LBW as a birth weight below 2500 grams,[1,2] with a global prevalence of 20 million cases annually, affecting 16.5% of births in developing nations compared to 7.0% in developed countries.[3,4] Due to immature metabolic adaptation, LBW neonates are more susceptible to complications in the immediate postnatal period.[5]

Hypoglycaemia, defined as blood glucose below 45 mg/dL,[6] occurs frequently in LBW, preterm, and intrauterine growth-restricted (IUGR) neonates due to limited glycogen reserves and immature glucose regulation.[7,8] It affects 1–5 per 1000 live births and 17% of NICU admissions, with small-for-gestational-age (SGA) and large-for-gestational-age (LGA) neonates at higher risk due to altered glucose utilization.[9,10]

Neonatal hypoglycaemia often presents with nonspecific or asymptomatic signs, such as jitteriness, lethargy, poor feeding, and apnea. If untreated, it can lead to long-term

neurodevelopmental consequences, including cognitive impairment and motor deficits. Studies indicate that even a single transient episode may impact neurological function later in life.[11,12,13,14]

Despite its clinical significance, no universal consensus exists regarding the ideal glucose threshold for intervention, particularly in resource-limited settings. Variability in screening and management further complicates diagnosis and treatment. Early detection and timely intervention are crucial for reducing complications. We aimed to examine the association between neonatal hypoglycemia and LBW, analyzing its prevalence, risk factors, and clinical implications. Our study contributed to refining screening protocols and management strategies, improving neonatal care, and reducing adverse outcomes in vulnerable newborns.

MATERIALS AND METHODS

Study Design and Setting

This prospective longitudinal study was conducted in the Paediatric Newborn Unit of T.S. MISRA Medical College and Hospital, Lucknow, over a period of 18 months (January 2022 – June 2023). The study focused on low birth weight (LBW) neonates to evaluate the prevalence, risk factors, and clinical implications of neonatal hypoglycaemia.

Study Population and Sample Size

The study included 58 neonates with LBW weighing less than 2500 grams. The sample size was calculated using a prevalence-based formula, yielding a minimum requirement of 57 neonates. However, 58 neonates were enrolled to ensure better statistical reliability.

Inclusion Criteria

1. Neonates weighing < 2.5 kg, irrespective of illness status.
2. Preterm or small-for-gestational-age (SGA) neonates.
3. SGA neonates below the 10th percentile for gestational age.

Exclusion Criteria

1. Neonates born to diabetic mothers.
2. Infants with congenital anomalies.
3. Cases where parents or guardians refused participation.

Data Collection and Study Procedure

Upon admission, neonates underwent detailed clinical evaluations, including anthropometric measurements, gestational age assessment, and systemic examination. Feeding was initiated based on gestational maturity, using direct breastfeeding, formula feeding via an orogastric tube, or intravenous glucose infusion (4-6 mg/kg/min) when oral feeding was not possible.

Blood glucose levels were monitored at specific time intervals: 2, 6, 12, 24, 48, and 72 hours post-delivery. Neonates with blood glucose levels of ≤40 mg/dL were classified as hypoglycaemic, and a confirmatory glucose oxidase test was performed using 3 mL of venous blood.

Laboratory Investigations

Blood glucose levels were assessed using two methods:

1. **Glucometer Method:** Heel-prick blood samples were placed on a test strip linked to the glucometer, which provided results within 4-5 seconds based on an enzymatic reaction at an electrode.
2. **Glucose Oxidase Method:** A 2 mL blood sample was treated with a sodium fluoride-potassium oxalate mixture, followed by centrifugation at 3000 rpm and incubation at 37°C for 7 minutes. The glucose concentration was then measured spectrophotometrically at 505 nm.

Additional laboratory investigations were conducted when necessary, including, Blood culture, Hemoglobin (Hb%), Differential Cell Count (DC), Total Leukocyte Count (TLC), Total Platelet Count (TPC), C-reactive Protein (CRP).

Statistical Analysis

Data were recorded in Microsoft Excel and analyzed using SPSS 25.0. Descriptive statistics (mean, standard deviation, frequency, percentage) summarized findings, while inferential tests (Chi-square, t-test, ANOVA) assessed significance. A p-value < 0.05 was considered statistically significant, with $p < 0.01$ and $p < 0.001$ indicating higher significance levels.

Ethical Considerations

The study received Institutional Ethics Committee approval, and informed consent was obtained from parents or guardians. Patient confidentiality and privacy were strictly maintained.

This study systematically evaluated neonatal hypoglycaemia in LBW infants, analyzing prevalence, risk factors, and clinical implications. The findings contributed to improving screening protocols and management strategies, enhancing neonatal care, and reducing adverse outcomes in vulnerable newborns.

RESULTS

Demographic and clinical characteristics of low birth weight (LBW) neonates and their mothers. The majority of neonates were preterm (63.8%), with 56.9% weighing between 1500-2500 grams. Males (51.7%) were slightly more prevalent than females. Caesarean deliveries (56.9%) were more frequent, and most mothers were under 35 years (79.3%). Multiparous mothers (65.5%) were more common compared to primiparous mothers as shown in Table 1.

Table 1: Neonatal and Maternal Characteristics in Low Birth Weight Neonates

Variables		No. of cases (n=58)	Percentage
Gender	**Male**	30	51.7%
	Females	28	48.3%
Gestation	**Preterm**	37	63.8%
	Term	21	36.2%
Birth weight in grams	**<1500**	25	43.1%
	1500-2500	33	56.9%
Weight for gestational age of baby	**AGA**	40	68.9%
	SGA	18	31.0%
Mode of Delivery	**Caesarean**	33	56.9%
	Vaginal	25	43.1%
Maternal Age in years	**< 35**	46	79.3%
	≥ 35	12	20.7%
Maternal Parity	**Primiparous**	20	34.5%
	Multiparous	38	65.5%

Key neonatal clinical parameters, including birth weight, heart rate, respiratory rate, blood pressure, first feed time, and glucose infusion rate. These parameters provide essential insights into the physiological status of neonates, helping guide clinical monitoring and management for better neonatal outcomes as shown in Table 2. [Table 2]

Table 2: Anthropometric profile, vital signs, and first feed time of the low-birth-weight infants enrolled in the study

Variables	Mean±SD
Birth weight in kilograms	1.9±0.4
Heart rate	139.1±13.2
Respiratory rate	48.0±12.0
SBP in mmHg	68.0±8.0
DBP mmHg	41.0±5.6
First Feed time (in hours)	17.8±12.6
Glucose infusion rate (mg/kg/minute)	4.3±1.0

Association between neonatal hypoglycaemia, birth weight categories, and gestational factors. The majority of hypoglycaemic neonates (66.7%) belonged to the low birth weight (1.51-2.5 kg) group, while preterm neonates (80%) had a significantly higher incidence compared to term neonates (p=0.024). Additionally, small-for-gestational-age (SGA) neonates (60%) were more frequently affected than appropriate-for-gestational-age (AGA) neonates (40%), with a statistically significant difference (p=0.015). This emphasizes the importance of early glucose monitoring and proactive management in neonates at risk as shown in Table 3. [Table 3]

Table 3: Neonatal Hypoglycaemia in Relation to Birth Weight and Gestational Age

Variables		Hypoglycaemic (n=15)	Normoglycemic (n=43)	p-value
Birth Weight (Kg)	**Extremely Low (≤1.0kg)**	1 (6.7%)	0 (0.0%)	0.171
	Very Low (1.001-1.5Kg)	4 (26.7%)	8 (18.6%)	
	Low (1.51-2.5 Kg)	10 (66.7%)	35 (81.4%)	
Birth Weight to Gestational Age	**SGA**	9 (60.0%)	11 (25.6%)	0.015
	AGA	6 (40.0%)	32 (74.4%)	
Gestational Age	**Term**	3 (20.0%)	23 (53.5%)	0.024
	Preterm	12 (80.0%)	20 (46.5%)	

The maternal, fetal, and neonatal risk factors associated with neonatal hypoglycaemia. Birth asphyxia (53.3%) was significantly associated with hypoglycaemia (p=0.017), while IUGR (26.7%) was also common among hypoglycaemic neonates. Intravenous feeding (80.0%) was more frequent in hypoglycaemic cases. Other maternal and fetal risk factors, including pre-eclampsia (13.3%) and PROM (6.7%), were observed but without statistical significance. This underscores the importance of early monitoring and intervention in high-risk neonates as shown in Table 4. [Table 4]

Table 4: Maternal, Fetal, and Neonatal Risk Factors for Hypoglycaemia

Variables		Hypoglycaemic (n=15)	Normoglycemic (n=43)	p-value
Maternal risk factors	**PROM**	1 (6.7%)	4 (9.3%)	0.754
	Pre-eclampsia	2 (13.3%)	13 (30.2%)	0.198
	Placental abnormality	0 (0.0%)	2 (4.6%)	0.395
	Maternal infection	1 (6.7%)	3 (6.9%)	0.964
Fetal Risk Factors	**Fetal Distress**	1 (6.7%)	1 (2.3%)	0.427
	IUGR	4 (26.7%)	13 (30.2%)	0.794
	Gemelli	1 (6.7%)	2 (4.6%)	0.762

Neonatal Factors	**Birth Asphyxia**	8 (53.3%)	9 (20.9%)	0.017
	Neonatal Jaundice	1 (6.7%)	8 (18.6%)	0.271
	Infection	1 (6.7%)	1 (2.3%)	0.427
	RDS	0 (0.0%)	1 (2.3%)	0.551
Type of Feed	**Intravenous**	2 (80.0%)	26 (60.5%)	0.192
	Intragastric	1 (6.7%)	1 (2.3%)	
	Oral	2 (13.3%)	16 (37.2%)	

The odds ratio and confidence intervals (CI) of various risk factors for neonatal hypoglycaemia. Gestational age (OR = 7.943, p < 0.001) had the strongest association with neonatal hypoglycaemia, indicating that preterm neonates were at significantly higher risk. Other factors, such as birth weight (OR = 3.833) and birth asphyxia (OR = 1.828), showed increased risk but were not statistically significant as shown in Table 5. This highlights the importance of targeted monitoring and early interventions for at-risk neonates. [Table 5]

Table 5: Multivariate logistic regression of risk factors for neonatal hypoglycaemia

Variables	Odd ratio (95.0% CI)	p-value
Gestational age	7.943 (3.911 to 16.130)	**<0.001**
Birth weight	3.833 (1.690 to 8.692)	0.113
Mode of delivery	0.752 (0.406 to 1.393)	0.365
Birth weight to gestational age	0.905 (0.357 to 2.294)	0.833
Maternal heart disease	0.545 (0.123 to 2.417)	0.424
Maternal infection	0.685 (0.180 to 2.604)	0.578
IUGR	1.630 (0.554 to 4.792)	0.374
Birth asphyxia	1.828 (0.898 to 3.724)	0.096
Neonatal jaundice	0.618 (0.228 to 1.675)	0.345
Neonatal infection	1.576 (0.482 to 5.157)	0.452

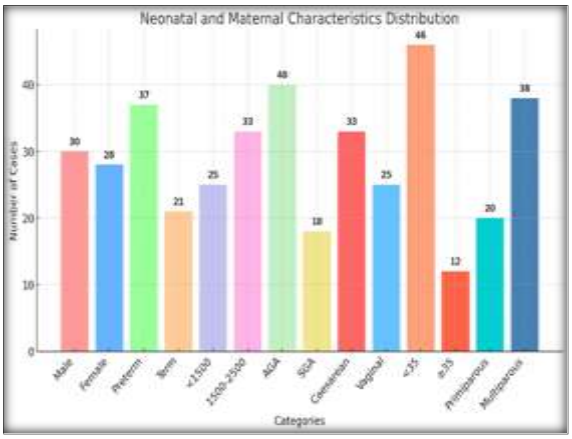

Figure 1

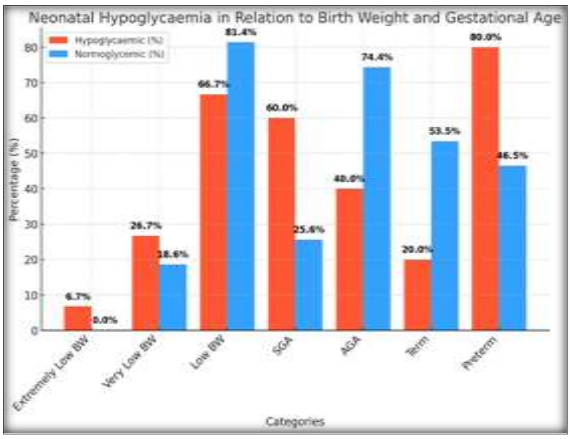

Figure 3:

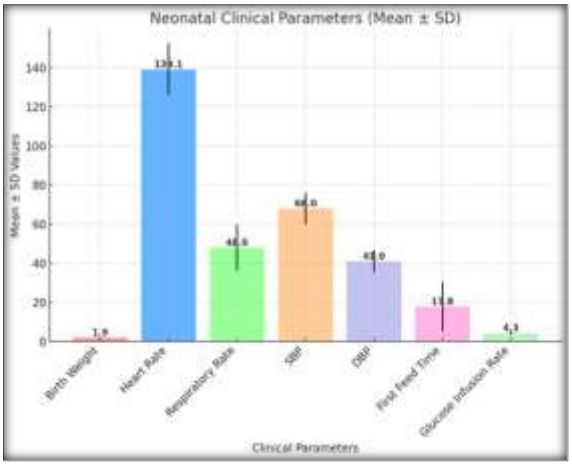

Figure 2

DISCUSSION

This study examined blood glucose levels and the occurrence of hypoglycaemia in low-birth-weight (LBW) neonates, analyzing its association with neonatal and maternal factors. The incidence of hypoglycaemia in our study was 25.8%, closely aligning with findings from Bhat R et al,[15] (32.5%), Siddique AA and Sridhar NL,[16] (30.0%), Yunarto Y et al,[17] (18.2%), and Osier FH et al,[18] (23.4%). Other studies have reported variable incidences, such as Dias E and Gada S,[19] (17%), Jonas D et al,[20] (11.7%), Yoon JY et al.21 (20.0%), and Dashti N et al,[22] (15.15%).

Among the 58 neonates, 51.7% were male, and 63.8% were preterm. A higher prevalence of hypoglycaemia (66.7%) was observed in neonates with low birth weight (1.51–2.5 kg), though no significant correlation was found (p>0.05), consistent with Siddique AA et al,[16] Bhat R et al,[15] and Saini

A et al,[23] who reported no significant association between birth weight and hypoglycaemia. Burdan DR et al,[24] and Hawdon JM et al,[25] identified LBW as a risk factor for hypoglycaemia, while Mejri A et al,[26] found no significant difference between neonates with BW below the 5th percentile and those between the 5th–10th percentile. A significant association was noted between SGA status and hypoglycaemia ($p<0.05$), with 60% of hypoglycaemic neonates being SGA, consistent with Ho J et al,[27] (34.2%), Yunarto Y et al,[17] (59.8%), and Holtrop PC28 (14.7%). Tom C et al,[29] found higher hypoglycaemia rates in SGA infants (66%) than AGA infants (30%). A study by Lubchenco LO,[30] also reported higher hypoglycaemia rates among SGA neonates.

Preterm birth was another significant factor, with 80.0% of hypoglycaemic neonates being preterm ($p<0.05$), consistent with findings from Ali BA et al,[31] Zhou Y et al,[32] Bromiker R et al,[33] and Naif MH et al,[34] all reporting an increased risk of hypoglycaemia in preterm neonates.

Our study found no significant association between maternal risk factors (PROM, pre-eclampsia, infection) and hypoglycaemia ($p>0.05$), in agreement with Yunarto Y et al.[17] However, Bhat R et al,[15] identified maternal diabetes, intrapartum fluids, and polycythemia as contributing factors. Somanathan S et al,[10] reported maternal diabetes (20.4%) and pregnancy-induced hypertension (14%) as risk factors, similar to Singhal PK et al,[35] (23.8%).

Birth asphyxia was significantly associated with hypoglycaemia ($p<0.05$), occurring in 53.3% of hypoglycaemic neonates, consistent with Yunarto Y et al,[17] (48.8%), Hosagasi NH et al,[36] (30%), and Somanathan S et al,[10] who identified perinatal asphyxia as a significant risk factor. Other conditions, such as neonatal jaundice, infection, and RDS, showed no significant association ($p>0.05$), aligning with Hosagasi NH et al.36 and Somanathan S et al,[10]

There was no significant difference in feeding type between hypoglycaemic and normoglycemic neonates ($p>0.05$). However, hypoglycaemia was more common in neonates receiving intravenous glucose (80%), similar to findings by Bhat R et al,[15] and Tom C et al,[29] who reported higher recurrent hypoglycaemia in preterm neonates on IV fluids.

CONCLUSION

Neonatal hypoglycaemia remains a significant concern in low birth weight (LBW) neonates, particularly among preterm and small-for-gestational-age (SGA) infants. Our study highlights the strong association between prematurity, birth asphyxia, and hypoglycaemia, emphasizing the need for early glucose monitoring and targeted interventions. While maternal risk factors were not significantly correlated, neonatal factors such as birth weight and feeding methods played crucial roles. Proactive management and continuous monitoring in high-risk neonates are essential to prevent complications and improve neonatal outcomes.

Strengths of the study

This study provides valuable insights into neonatal hypoglycaemia in LBW infants, emphasizing its association with gestational age, birth weight, and neonatal factors. The use of multivariate analysis strengthens the findings. Additionally, the study's prospective design ensures reliable data collection and enhances the accuracy of risk factor evaluation.

Limitations of the study

The study was limited to NICU-admitted neonates, potentially affecting generalizability. Outborn infants and persistent hypoglycaemia cases were excluded, possibly underestimating the true incidence. The sample size was relatively small, and maternal glucose levels were not assessed, which could have provided further insights into neonatal hypoglycaemia risks.

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Ethical Approval: Obtained.

Consent: Written consent secured.

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