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SERUM GLUCOSE AND CALCIUM LEVELS IN TERM NEONATES WITH BIRTH ASPHYXIA AND THEIR VARIATION WITH SEVERITY: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Birth asphyxia is a major contributor to neonatal mortality and morbidity. Biochemical disturbances including hypoglycaemia and hypocalcaemia are recognised complications that may worsen neurological outcomes if not identified early. This study compared serum glucose and calcium levels in term neonates with and without birth asphyxia and examined their variation with asphyxia severity. **Methods:** A single-centre, hospital-based, two-group, prospective observational study was conducted at the Neonatal Intensive Care Unit of Amaltas Institute of Medical Sciences, Dewas. A total of 80 term neonates were enrolled: 40 with birth asphyxia (Apgar score <7 at 1 minute) and 40 healthy term controls. Serum glucose and total serum calcium and ionized calcium were measured at 24 hours of life. Asphyxia was classified as mild, moderate, or severe using Apgar scores and neurological assessment. Group comparisons used independent t-test and chi-square test.**Results:** Mean serum glucose was significantly lower in the asphyxia group (47.3±10 vs 62±8.05 mg/dL; p = 0.003). Hypoglycaemia was present in 20% of asphyxiated neonates versus 2.5% of controls (p = 0.007). Total serum calcium (7.49±0.845 vs 8.67±0.98 mg/dL) and ionized calcium (3.88±0.4 vs 4.54±0.531 mg/dL) were both significantly lower in the asphyxia group (p < 0.0001 for both). Hypocalcaemia was present in 22.5% of asphyxiated neonates versus 5% of controls (p = 0.042). Serum glucose declined progressively with increasing asphyxia severity (p = 0.004); calcium levels remained reduced across all severity categories (p = 0.009). Hypoglycaemia reached 57.1% in severe asphyxia (p = 0.012).**Conclusion:** Hypoglycaemia and hypocalcaemia are significantly more frequent in term neonates with birth asphyxia and increase with severity. Routine biochemical monitoring of serum glucose and calcium at 24 hours is essential in all asphyxiated neonates, particularly in severe cases, to enable timely intervention and potentially reduce secondary neurological injury.

KEYWORDS

Birth Asphyxia; Neonatal Hypoglycaemia; Neonatal Hypocalcaemia; Serum Glucose; Serum Calcium; Apgar Score; Nicu

INTRODUCTION

Birth asphyxia remains one of the leading causes of neonatal mortality and long-term neurodevelopmental disability worldwide. The World Health Organization defines it as the failure to initiate and sustain breathing at birth, resulting from impaired gas exchange that leads to hypoxia, hypercapnia, and metabolic acidosis.[1,2] Globally, birth asphyxia accounts for approximately 23% of all neonatal deaths, and the burden is disproportionately higher in low- and middle-income countries where access to skilled intrapartum care is limited.[3] In India, the incidence is estimated at 3–8 per 1000 live births, and it remains a major contributor to the national perinatal mortality rate.[4] Beyond immediate mortality, asphyxia causes a cascade of organ dysfunction that affects the brain, kidneys, heart, liver, and gastrointestinal system. The neurological sequelae, broadly termed hypoxic-ischaemic encephalopathy (HIE), range from transient behavioural abnormalities to severe, permanent impairment.[5] Among the biochemical disturbances that accompany asphyxia, alterations in serum glucose and calcium metabolism are particularly relevant to clinical management. Cerebral metabolic demand increases during hypoxia, accelerating glucose consumption and depleting glycogen stores, while simultaneously impairing gluconeogenesis. This predisposes asphyxiated neonates to hypoglycaemia, which can independently worsen neuronal injury.[6,7]

Hypocalcaemia, defined as total serum calcium below 7 mg/dL in term neonates, is another recognised complication of birth asphyxia. The proposed mechanisms include elevated calcitonin secretion, altered parathyroid hormone response to hypoxia, intracellular calcium redistribution following cellular injury, and hypomagnesaemia-induced impairment of parathyroid function.[8,9] Both hypoglycaemia and hypocalcaemia, if left uncorrected, can exacerbate neuronal damage, precipitate seizures, and worsen cardiac function. Despite their clinical importance, these biochemical disturbances are not always systematically screened in resource-limited NICU settings. Several studies have examined serum glucose and calcium in asphyxiated neonates, but most are retrospective, use different diagnostic thresholds, or do not examine severity-based gradations. Data from central India are limited. The present study was designed to prospectively compare serum glucose and total and ionized calcium levels between asphyxiated term neonates and healthy controls at 24 hours of life, and to assess how these parameters change across mild, moderate, and severe asphyxia.

Aim

To assess and compare serum calcium and serum glucose levels in term neonates with and without birth asphyxia, and to examine their variation across different degrees of asphyxia severity.

Material and Methods

This was a single-centre, hospital-based, two-group, prospective observational study. The study was conducted in the Neonatal Intensive Care Unit, Department of Paediatrics, Amaltas Institute of Medical Sciences, Dewas, Madhya Pradesh, in collaboration with the Department of Obstetrics and Gynaecology. The study was conducted over 18 months, with 12 months dedicated to participant recruitment and data collection. Ethical clearance was obtained from the Institutional Ethics Committee of Amaltas Institute of Medical Sciences prior to commencement of the study. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the parents or legally acceptable representatives of all enrolled neonates before enrolment, in the language of their preference.

The primary outcomes were serum glucose and serum calcium (total and ionized) levels measured at 24 hours of life, compared between asphyxiated and non-asphyxiated term neonates. Secondary outcomes included the prevalence of hypoglycaemia and hypocalcaemia, and the variation of these parameters across mild, moderate, and severe asphyxia. Hypoglycaemia was defined as serum glucose <40 mg/dL; hypocalcaemia as total serum calcium <7 mg/dL. Severity of asphyxia was graded using Apgar scores at 1 and 5 minutes combined with neurological assessment: mild (Apgar 5–6), moderate (Apgar 3–4), severe (Apgar ≤2).

Study Group: Term neonates with birth asphyxia, defined by Apgar score <7 at 1 minute (n = 40). Control Group: Healthy term neonates without asphyxia, with Apgar scores ≥7 at 1 minute (n = 40). Allocation was non-randomised and based strictly on clinical status at birth and Apgar scoring.

Inclusion Criteria:

1. Term neonates (gestational age 37–42 weeks).
2. Birth weight >1500 grams.
3. Delivered at Amaltas Institute of Medical Sciences.
4. Written informed consent provided by parents or guardian.

Exclusion Criteria:

1. Preterm neonates (<37 weeks of gestation).
2. Neonates with congenital malformations.
3. Neonates born to mothers with diabetes mellitus or toxaemia of pregnancy.
4. Neonates born to mothers with severe vitamin D deficiency.
5. Neonates born to mothers with hyperparathyroidism.
6. Neonates born to mothers taking anticonvulsants (phenobarbitone or sodium valproate).
7. Neonates born to mothers with a history of high-dose antacid intake.

The minimum sample size was calculated using the formula $N = Z^2 \times P(1-P) / d^2$, where Z = 1.96, P = 0.028, and d = 0.05, yielding a minimum of 40 neonates per group. A non-random convenience sampling method was used; eligible neonates admitted to the NICU during the study period were screened consecutively and enrolled until the required sample was reached.

Data Collection Procedure

Following enrolment, a structured close-ended proforma was completed for each participant, capturing maternal details, perinatal history, delivery information, Apgar scores, and clinical examination findings. Clinical assessment included neurological status, tone, reflexes, and systemic examination. Venous blood (2 ml) was collected under aseptic precautions at 24 hours of life. Serum glucose was measured by the glucose oxidase-peroxidase (GOD-POD) method; total serum calcium by the o-cresolphthalein complexone (OCPC) method; and ionized calcium was calculated. All analyses were performed in the institutional accredited laboratory with internal quality control. The overall incidence of birth asphyxia during the study period was calculated from institutional birth records.

Statistical Analysis:

Data were analysed using Stata version 17.0. Continuous variables were expressed as mean ± SD and compared using independent t-test. Categorical variables were expressed as frequencies and percentages and compared using Pearson chi-square test. Severity-based comparisons used one-way ANOVA for continuous variables and chi-square test for categorical data. A p-value of <0.05 was considered statistically significant.

RESULTS

Birth asphyxia occurred in 108 of 748 live births at the institute (14.43%) during the study period. Of these, 40 were term neonates (included in the present study) and 68 were preterm. This overall incidence is notably high compared to national averages, reflecting the tertiary referral nature of the centre and the profile of high-risk deliveries it receives.

A total of 80 term neonates were enrolled and analysed: 40 in the asphyxiated group and 40 healthy controls. All participants had complete data for the primary outcomes. The detailed findings are presented below.

Table 1: Characteristics of Participants

Characteristic	Controls (n=40)		Asphyxia (n=40)	
	n	%	n	%
Gestational Age (weeks)				
37	5	12.5	6	15.0
38	3	7.5	6	15.0
39	5	12.5	8	20.0
40	10	25.0	8	20.0
41	7	17.5	7	17.5
42	10	25.0	5	12.5
Gender				
Male	26	65.0	16	40.0
Female	14	35.0	24	60.0
Birth Weight				
Low birth weight (1500–2499 g)	14	35.0	9	22.5
Normal birth weight (2500–3999 g)	26	65.0	31	77.5
Mean birth weight: Controls 2818 ± 551 g | Asphyxia 2944 ± 408 g				

Table 1 presents the baseline characteristics of both groups. Gestational age distribution differed slightly, with more controls at 40–42 weeks (50%) and more asphyxiated neonates at 37–39 weeks (50%). Female neonates predominated in the asphyxia group (60%) while males predominated in the control group (65%). Normal birth weight was more common in both groups (65% and 77.5%), with a slightly higher mean birth weight in the asphyxia group (2944±408 vs 2818±551 g).

Table 2: Severity Distribution in the Asphyxia Group

Severity of Asphyxia	Controls (n=40)		Asphyxia n=40	
	n	%	n	%
None	40	100	0	0
Mild (Apgar 5–6 at 1 min)	0	0	20	50.0
Moderate (Apgar 3–4 at 1 min)	0	0	13	32.5
Severe (Apgar ≤2 at 1 min)	0	0	7	17.5

Table 2 shows the distribution of asphyxia severity. All 40 controls had no asphyxia. Among the 40 asphyxiated neonates, 20 (50%) had mild, 13 (32.5%) had moderate, and 7 (17.5%) had severe asphyxia. Mild asphyxia was the predominant category, with severe asphyxia least common, consistent with the referral profile of a tertiary NICU.

Table 3: Serum Glucose, Total Calcium, and Ionized Calcium at 24 Hours

Biochemical Parameter	Controls Mean	Controls SD	Asphyxia Mean	Asphyxia SD	P-value
Serum glucose at 24h (mg/dL)	62	8.05	47.3	8.9	0. 003
Total serum calcium at 24h (mg/dL)	8.67	0.98	7.49	0.845	< 0.001
Ionized calcium at 24h (mg/dL)	4.54	0.531	3.88	0.4	< 0.001

Table 3 shows that all three biochemical parameters were significantly lower in the asphyxia group. Mean serum glucose was 47.3±10 mg/dL in the asphyxia group versus 62±8.05 mg/dL in controls (p = 0.003). Total serum calcium was 7.49±0.845 versus 8.67±0.98 mg/dL (p < 0.0001). Ionized calcium was 3.88±0.4 versus 4.54±0.531 mg/dL (p < 0.0001). Both calcium parameters showed stronger statistical significance than glucose, reflecting the predominance of calcium-disrupting mechanisms in asphyxia.

Table 4: Prevalence of Hypoglycaemia and Hypocalcaemia

Electrolyte Abnormality	Controls (n=40)		Asphyxia n=40		P-value
	n	%	n	%	
Hypoglycaemia (<40 mg/dL)	1	2.5	8	20.0	0.007
Hypocalcaemia (<7 mg/dL)	2	5.0	9	22.5	0.042

Table 4 shows that hypoglycaemia was present in 20% of asphyxiated neonates versus 2.5% of controls (p = 0.007). Hypocalcaemia was present in 22.5% of asphyxiated neonates versus 5% of controls (p = 0.042). Both abnormalities were significantly more frequent in the asphyxia group, with hypocalcaemia being the more common categorical electrolyte finding.

Table 5: Serum Glucose and Calcium by Severity of Asphyxia

Parameter	None n=40	Mild n=20	Mod n=13	Severe n=7	P-value
Serum glucose (mg/dL)	62 ± 8.05	50.1 ± 8.41	48.1± 7.04	37.5 ±13.7	0.004
Total serum calcium (mg/dL)	8.67 ± 0.98	7.58 ± 0.96	7.68 ± 0.69	7.25 ±0.71	0.009
Ionized calcium (mg/dL)	4.54 ± 0.531	3.96 ± 0.428	3.77 ± 0.353	3.87 ±0.40	0.013

Table 5 shows severity-based trends. Serum glucose declined progressively from 62±8.05 (no asphyxia) to 50.1±8.41 (mild), 48.1±7.04 (moderate), and 37.5±13.7 (severe; p = 0.004). Total calcium was lower in all asphyxia severity groups compared to

controls, with the lowest mean in severe asphyxia (7.25±0.71; p = 0.009). Ionized calcium also showed lower values across all severity categories (p = 0.013). The progressive decline in serum glucose with worsening severity is a clinically notable finding.

Table 6: Prevalence of Hypoglycaemia and Hypocalcaemia Across Severity Groups

Abnormality	None n=40 n (%)	Mild n=20 n (%)	Moderate n=13 n (%)	Severe n=7 n (%)	P-value
Hypoglycaemia (<40 mg/dL)	1 (2.5)	2 (10.0)	2 (15.4)	4 (57.1)	0.012
Hypocalcaemia (<7 mg/dL)	2 (5.0)	5 (25.0)	3 (23.1)	1 (14.3)	0.019

Table 6 shows severity-stratified categorical abnormality rates. Hypoglycaemia rose sharply with severity: 2.5% (none), 10% (mild), 15.4% (moderate), and 57.1% (severe; p = 0.012). Hypocalcaemia followed a different pattern, with higher rates in mild (25%) and moderate (23.1%) cases than in severe (14.3%) asphyxia, though the overall association was significant (p = 0.019). The severity-dependent rise in hypoglycaemia is clinically important, as 57.1% of neonates with severe asphyxia had dangerous glucose levels.

DISCUSSION

This prospective study enrolled 80 term neonates: 40 with birth asphyxia and 40 healthy controls in the NICU of Amaltas Institute of Medical Sciences, Dewas. Serum glucose, total calcium, and ionized calcium were measured at 24 hours of life. All three parameters were significantly lower in the asphyxia group, and both hypoglycaemia and hypocalcaemia were significantly more prevalent. Severity-based analysis showed that glucose declined progressively with increasing asphyxia, while calcium remained broadly reduced across all severity categories. The findings confirm the clinical importance of routine biochemical monitoring in asphyxiated neonates from the first day of life.

The overall incidence of birth asphyxia at the institute during the study period was 14.43%, which is higher than the national estimate of 3–8 per 1000 live births.[4] This elevated rate reflects the tertiary referral profile of Amaltas Institute, which receives high-risk obstetric cases from surrounding districts of Madhya Pradesh. Among the 108 affected neonates, 40 were term and 68 preterm; only term neonates were included in the present study to eliminate gestational age as a confounding variable. This selective inclusion strengthens the internal validity of the biochemical comparisons.

Mean serum glucose was significantly lower in asphyxiated neonates (47.3±10 vs 62±8.05 mg/dL; p = 0.003), and hypoglycaemia was present in 20% versus 2.5% of controls (p = 0.007). The physiological basis is well-established: hypoxia accelerates anaerobic glycolysis, depleting hepatic glycogen stores while simultaneously impairing gluconeogenesis and increasing peripheral glucose consumption. Reduced oral intake compounds the deficit.[6,7] These findings are consistent with Rai S et al. (2015), who reported mean serum glucose of 54.4±10.91 mg/dL in asphyxiated neonates versus 76±15.5 mg/dL in controls, with a significant decline across severity categories.[10] Lahari DSS et al. (2024) found a mean glucose of 44.43±6.5 mg/dL in asphyxiated neonates, with the lowest values in severe HIE (38.12±4.65 mg/dL),[11] closely mirroring the present finding of 37.5±13.7 mg/dL in severe asphyxia. Solanki A et al. (2025) also reported significantly lower glucose levels in asphyxiated neonates compared to controls (p < 0.001).[12] The 20% rate of hypoglycaemia in the present study is comparable to the 20% reported by Lahari DSS et al. (2024), suggesting consistent prevalence across similar tertiary care settings in India.

The severity-dependent decline in glucose is particularly clinically important. Hypoglycaemia reached 57.1% in the severe asphyxia subgroup (p = 0.012). Since hypoglycaemia independently exacerbates neuronal injury by depriving vulnerable neurons of their primary energy substrate,[6] the high prevalence in severe cases underscores the critical need for glucose monitoring and correction from the first hours of NICU admission in all asphyxiated neonates, not only those with clinical signs.

Total serum calcium (7.49±0.845 vs 8.67±0.98 mg/dL; p < 0.0001) and ionized calcium (3.88±0.4 vs 4.54±0.531 mg/dL; p < 0.0001) were both highly significantly lower in asphyxiated neonates. Hypocalcaemia was present in 22.5% of the asphyxia group versus 5% of controls (p = 0.042). These findings reflect multiple interacting mechanisms: perinatal hypoxia elevates calcitonin levels, which suppress calcium mobilisation from bone; impaired parathyroid hormone response reduces intestinal calcium absorption; intracellular calcium shifts during cellular injury deplete the extracellular pool; and associated hypomagnesaemia may further blunt parathyroid hormone secretion.[8,9] Rai S et al. (2015) reported significantly lower mean serum calcium in asphyxiated neonates (8.31±0.48 vs 9.47±0.49 mg/dL), with a progressive decline across severity.[10] Solanki A et al. (2025) found mean serum calcium of 7.12±0.65 mg/dL in asphyxiated neonates versus 8.42±0.52 mg/dL in controls, with hypocalcaemia in 45% of the asphyxia group,[12] a higher rate than the present 22.5%, possibly reflecting a population with greater severity at presentation. Lahari DSS et al. (2024) documented mean total calcium of 7.87±1.87 mg/dL and ionized calcium of 3.27±0.76 mg/dL in asphyxiated neonates, with calcium declining significantly with HIE stage.[11] Jajoo et al. (1995) reported mean calcium of 7.64±0.59 mg/dL with a decreasing trend across severity stages,[13] consistent with the present study.

The pattern of hypocalcaemia across severity groups in the present study showed a non-linear distribution: rates were 25% in mild, 23.1% in moderate, and 14.3% in severe asphyxia. This pattern may reflect survivorship bias — severely asphyxiated neonates with the most profound calcium depletion may not survive long enough to be sampled at 24 hours — or it may indicate that calcium responses are not strictly linearly proportional to the degree of hypoxia. Hassan M et al. (2022) reported a progressive decline in calcium from 7.89 in stage I to 6.88 in stage III HIE,[14] which contrasts slightly with the present finding. The difference may reflect variations in timing of sampling relative to asphyxia onset, gestational age composition, and definitions used. The clinical significance of hypocalcaemia in asphyxiated neonates lies in its effects on neuromuscular excitability, cardiac contractility, and its potential to precipitate seizures. In a neonate already at risk for HIE-related seizures, superimposed hypocalcaemia increases the seizure threshold and worsens neurological outcomes. Early correction with calcium gluconate is both safe and effective, but requires prior identification through biochemical monitoring.

The findings of the present study support the inclusion of serum glucose and calcium in the routine biochemical monitoring protocol for all term neonates with birth asphyxia. Monitoring at 24 hours of life — the time point used in this study — captures the peak metabolic vulnerability period. Given that 57.1% of neonates with severe asphyxia had hypoglycaemia and up to 25% with mild asphyxia had hypocalcaemia, monitoring should not be restricted to the most severely affected cases. Both parameters are inexpensive, widely available, and easily correctable. Early identification and treatment may reduce the additive burden of metabolic injury on an already compromised neonatal brain.

CONCLUSION

Serum glucose (p = 0.003), total serum calcium (p < 0.0001), and ionized calcium (p < 0.0001) were all significantly lower in term neonates with birth asphyxia compared to healthy controls at 24 hours of life. Hypoglycaemia (20% vs 2.5%; p = 0.007) and hypocalcaemia (22.5% vs 5%; p = 0.042) were significantly more prevalent in asphyxiated neonates. Serum glucose declined progressively with increasing asphyxia severity, reaching 37.5±13.7 mg/dL in severe cases, and hypoglycaemia was present in 57.1% of severe cases (p = 0.012). Calcium levels remained reduced across all severity categories. These findings support routine biochemical monitoring of serum glucose and calcium at 24 hours of life in all term neonates with birth asphyxia, with particular urgency in severe cases, to enable timely correction and reduce secondary metabolic injury.

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Conflict of Interest:
The authors declare no conflicts of interest in the design, conduct, analysis, or reporting of this study.

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