Original Article
DOI: https://doi.org/10.70749/ijbr.v3i7.3111

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://ijbr.com.pk
ISSN: 2960-2793/ 2960-2807

Comparison of Serum Calcium Level in Neonates with and Without Birth Asphyxia

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ARTICLE INFO

Keywords: Asphyxia Neonatorum, Calcium, Hypocalcaemia, Infant Newborn, Neonatal Screening, Serum Calcium.

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Declaration
Authors' Contribution
All authors equally contributed to the study and approved the final manuscript

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History
Received: 07-06-2025 Revised: 29-06-2025
Accepted: 07-07-2025 Published: 10-07-2025

ABSTRACT

Background: Birth asphyxia is an important neonatal problem which may lead to metabolic disturbance including hypocalcaemia. Reduced serum calcium levels in asphyxiated neonates may increase risk of neurological and systemic complications during early neonatal period. **Objective:** To compare serum calcium level in neonates with and without birth asphyxia. **Study Design:** Case control study. **Duration and Place of Study:** This study was carried out from 7th December 2024 to 7th May 2025 in the Department of Paediatrics, Benazir Bhutto Hospital Rawalpindi. **Methodology:** A total of 46 term neonates were included, with 23 neonates in each group. Neonates with Apgar score ≤6 at 5 minutes along with clinical findings of asphyxia were included as cases, while neonates with Apgar score ≥7 and normal delivery findings were taken as controls. Cord blood sample of 2 mL was collected under sterile precautions for estimation of serum calcium level. Demographic variables were also recorded. Data was analysed by Statistical Package for Social Sciences version 25.0. **Results:** Mean serum calcium level was significantly lower in neonates with birth asphyxia (7.73 ± 0.46 mg/dL) compared to neonates without birth asphyxia (9.38 ± 0.38 mg/dL). The difference was statistically highly significant ($t = -13.255$, $p < 0.001$). Male neonates were 15 (65.2%) in both groups. Lower segment caesarean section was more common in case group 13 (56.5%), while normal vaginal delivery was more frequent in controls 16 (69.6%). **Conclusion:** Neonates with birth asphyxia had markedly lower serum calcium levels than non-asphyxiated neonates. Early assessment of serum calcium may help in timely diagnosis

INTRODUCTION

Birth asphyxia is one of the serious neonatal complications defined by the difficulty or failure to develop adequate respiration at birth which results in decreased oxygen supply and perfusion of the vital organs.[1] Birth asphyxia often arises due to prolonged labor, placental dysfunction, cord prolapse, and factors related to the mother, including hypertension and anemia.[2] Asphyxia affects various organ systems of an infant, particularly brain, heart, and kidneys which cause high mortality rate in the first weeks after birth.[3] In terms of clinical presentation, the patients demonstrate poor Apgar scores, reduced muscle activity, weakened crying, and slow reflexive responses.[4] Asphyxia can be mild, moderate, or severe; in severe cases, infants may develop hypoxic-ischemic encephalopathy.

Calcium levels in the serum of neonates represent one of the critical biochemical indices with implications for neuro-muscular excitability, cardiac muscle action, and enzyme activity.[5] Neonates that undergo asphyxia during delivery often suffer from deranged calcium metabolism owing to hypoxic damage to the parathyroid glands and the kidneys.[6] This results in poor availability of calcium and low serum levels of calcium and causes hypocalcemia. Symptoms of hypocalcemia in these neonates include twitching, convulsions, apnoea, or difficulty in feeding but can be asymptomatic and identified only by laboratory investigations.[7] The disturbance is more prominent during the first three days after delivery.

Non-asphyxiated newborns usually maintain steady levels of serum calcium, which is mainly due to the intact regulatory physiological mechanisms.[8] Both the parathormone reaction and the kidneys are functioning normally, allowing for adequate maintenance of calcium metabolism in the postpartum stage.[9] Although physiological hypocalcemia may be present in the initial stages of the neonatal period, it is usually of mild intensity and does not lead to any serious medical implications. Compared to asphyxiated newborns, non-asphyxiated

newborns rarely suffer from hypocalcemia and its possible repercussions.[10]

Birth asphyxia continues to be one of the major causes of morbidity and mortality among newborns, and their metabolic complications are usually underrated in clinical practice. Metabolic disorders such as alterations in serum calcium have a negative impact on neurological function, but this issue is usually disregarded when dealing with newborns suffering from birth asphyxia. However, there is inadequate local evidence regarding differences in serum calcium levels between newborns with and without birth asphyxia. Therefore this study is needed to assess and compare serum calcium levels in both groups in order to improve early detection and management of hypocalcaemia.

METHODOLOGY

This case control study was carried out in the Department of Pediatrics Benazir Bhutto Hospital, Rawalpindi from 7th December 2024 to 7th May 2025. Ethical approval was obtained from Institutional Ethical Review Committee and CPSP before start of the study. The sample size was calculated by using OpenEPI calculator for comparison of two means with 95% confidence level and 90% power of study. Anticipated mean serum Calcium level in neonates with birth asphyxia was 8.5 ± 1.67 and in neonates without birth asphyxia was 9.6 ± 0.27.[11] Total sample size was 46 neonates, with 23 neonates in each group.

Inclusion criteria: All the term neonates of both gender having birth weight >2.5 kg and age from birth to 28 days of life were included in the study. Controls included neonates with birth weight >2.5 kg, Apgar score ≥7 at 5 minutes of birth, normal fetal heart rate and clear amniotic fluid.

Exclusion criteria: Neonates having birth anomalies or suspected inborn errors of metabolism were excluded from study. Neonates born to mothers taking diuretics, antihypertensive drugs, hypoglycaemic drugs, phenobarbitone, pethidine, MgSO4, or any medicines causing neonatal respiratory distress were also excluded. Mothers having history of pregnancy induced hypertension, eclampsia, or maternal pyrexia within two weeks before delivery were also excluded from the study.

Written informed consent was taken from parents or attendants before inclusion in the study. They were informed regarding objectives of the study and confidentiality of information was ensured. Demographic details including age, gender, weight, parity, type of delivery, Apgar score, and calcium supplements during pregnancy were recorded.

Term neonates were labelled as babies born between 37 and 42 weeks of gestation. Birth asphyxia cases were labelled as neonates having Apgar score ≤6 at 5 minutes of birth along with minimum two or more findings including blood pH ≤7.2, abnormal fetal heart rate (<100/min or >160/min), meconium stained amniotic fluid, seizures, coma, or requirement of resuscitation with more than 1 minute of positive pressure ventilation. Controls were labelled as neonates having Apgar score ≥7 at 5 minutes of birth with normal fetal heart rate and clear amniotic fluid.

Following enrolment, 2 mL of the neonate's cord blood sample was drawn from each baby under sterile conditions and was placed into suitable containers. The samples were taken to the laboratory in the hospital for separation of the serum for determination of serum calcium levels. The average serum calcium level was chosen as the outcome measure for comparison among the two groups.

Data was analysed by using SPSS version 25.0. Quantitative variables including age, weight, APGAR score and Calcium level were presented as mean ± standard deviation. Qualitative variables including gender, type of delivery, parity and calcium supplements during pregnancy were presented as frequency and percentages. Independent sample t test was applied for comparison of mean Calcium level between both groups. Effect modifiers including gender, age, weight, parity, type of delivery, APGAR score and calcium supplements during pregnancy were controlled through stratification. Post stratification independent sample t test was applied to assess their effect on outcome. P value <0.05 was considered statistically significant.

RESULTS

The mean age of neonates in the case group was 7.91 ± 3.93 days, which was notably lower than in the control group where mean age was 21.13 ± 4.67 days. Mean birth weight in the case group was recorded as 2.85 ± 0.18 kg, compared to 3.23 ± 0.16 kg in the control group. The APGAR score at 5 minutes was considerably lower in the case group (4.70 ± 0.97) as compared to the control group (8.17 ± 0.78). Gender distribution was identical in both groups, with 15 males (65.2%) and 8 females (34.8%) in each. Regarding parity, majority of the cases were born to multiparous mothers — 17 (73.9%) in the case group and 14 (60.9%) in the control group, whereas primiparious mothers accounted for 6 (26.1%) and 9 (39.1%) in respective groups. Mode of delivery showed considerable variation between the groups; normal delivery was more frequent in the control group with 16 neonates (69.6%), whilst in the case group only 3 (13.0%) were delivered normally. Lower segment caesarean section (LSCS) was performed in 13 (56.5%) cases and 7 (30.4%) controls, and instrumental delivery was observed only in case group, accounting for 7 (30.4%) neonates. With respect to maternal calcium supplementation, majority of the control group mothers had received supplements — 20 (87.0%) — whereas only 7 (30.4%) mothers in the case group had received the same (Table-I).

Table I

Patient Demographics in Both Groups

Variables	With Birth Asphyxia n=23	Without Birth Asphyxia n=23
	Mean ± SD	Mean ± SD
Age (days)	7.91 ± 3.93	21.13 ± 4.67
Birth Weight (kg)	2.85 ± 0.18	3.23 ± 0.16
APGAR Score at 5 min	4.70 ± 0.97	8.17 ± 0.78
Gender	**n (%)**	**n (%)**
Male	15 (65.2%)	15 (65.2%)
Female	8 (34.8%)	8 (34.8%)
Parity	**n (%)**	**n (%)**
Primi	6 (26.1%)	9 (39.1%)
Multi	17 (73.9%)	14 (60.9%)
Mode of Delivery	**n (%)**	**n (%)**
Normal	3 (13.0%)	16 (69.6%)

LSCS	13 (56.5%)	7 (30.4%)
Instrumental	7 (30.4%)	0 (0.0%)
Calcium Supplements	**n (%)**	**n (%)**
Yes	7 (30.4%)	20 (87.0%)
No	16 (69.6%)	3 (13.0%)

The mean serum calcium level was significantly lower in neonates with birth asphyxia (7.73 ± 0.46 mg/dL) as compared to those without birth asphyxia (9.38 ± 0.38 mg/dL). The difference between the two groups were found to be statistically highly significant (t = −13.255, p <0.001), which suggesting that birth asphyxia is associated with considerably reduced serum calcium levels in neonates (Table-II).

Table II

Comparison of Mean Serum Calcium Level in Both Groups

	Case Group (With Birth Asphyxia) n=23	Control Group (Without Birth Asphyxia) n=23	t	P value
Serum Calcium Level (mg/dL)	7.73 ± 0.46	9.38 ± 0.38	-13.255	<0.001

When serum calcium levels were stratified by demographic variables, significant differences were observed across all subgroups analysed. In neonates aged ≤14 days, the case group (n=22) had a mean serum calcium of 7.72 ± 0.47 mg/dL compared to 8.9 mg/dL in the single control (p = 0.024). In those aged >14 days, the control group (n=22) showed a mean of 9.4 ± 0.37 mg/dL versus 7.9 mg/dL in the single asphyxiated neonate (p <0.001). Among male neonates, the mean serum calcium in case group (n=15) was 7.63 ± 0.5 mg/dL against 9.43 ± 0.36 mg/dL in the control group (p <0.001), and among females, values were 7.91 ± 0.35 mg/dL versus 9.29 ± 0.42 mg/dL respectively (p <0.001). In neonates whose mothers had received calcium supplementation, the case group mean was 7.89 ± 0.41 mg/dL compared to 9.35 ± 0.39 mg/dL in controls (p <0.001), and in those without supplementation, the case group recorded 7.66 ± 0.48 mg/dL versus 9.63 ± 0.23 mg/dL in the control group (p <0.001) (Table-III).

Table III

Stratification of Mean Serum Calcium Level with Respect to Demographic Factors in Both Groups

Demographic Factors	Group		Mean	SD	p Value*
Age (days)	≤14 days	Case Group (n=22)	7.72	0.47	0.024
		Control Group (n=1)	8.9	—	
	>14 days	Case Group (n=1)	7.9	—	<0.001
		Control Group (n=22)	9.4	0.37	
Gender	Male	Case Group (n=15)	7.63	0.5	<0.001
		Control Group (n=15)	9.43	0.36	
	Female	Case Group (n=8)	7.91	0.35	<0.001
		Control Group (n=8)	9.29	0.42	
Mother Calcium Supplements	Yes	Case Group (n=7)	7.89	0.41	<0.001
		Control Group (n=20)	9.35	0.39	
	No	Case Group (n=16)	7.66	0.48	<0.001
		Control Group (n=3)	9.63	0.23	

***Independent Sample t Test**

DISCUSSION

In this study, male neonates were predominant in both groups, comprising 15 (65.2%) in each, which is consistent with the general observation that male neonates are more vulnerable to perinatal complications due to relatively slower lung maturity and lesser hormonal protection as compared to females. There was a significantly high percentage of LSCS and instrumental delivery among neonates belonging to the case group (13 neonates 56.5% and 7 neonates 30.4%, respectively) compared to the controls with predominantly normal vaginal deliveries (16 neonates 69.6%). This implies that complicated or operative deliveries have higher risk of being associated with birth asphyxia, most probably related to complications such as prolonged labor, cord compression, and foeto-pelvic disproportion that may affect fetal oxygenation during delivery. Mean serum calcium concentration was significantly lower among babies who had birth asphyxia (7.73±0.46 mg/dl) than those without birth asphyxia (9.38±0.38 mg/dl) at p<0.001. The mechanism for this is based on the concept that during asphyxia there will be increased calcitonin production, decreased parathyroid hormone function, acidosis-induced cellular movement of calcium, all of which lead to reduction in the serum ionized calcium concentration. Furthermore, hypoxia-induced renal damage leads to decreased activation of vitamin D which affects intestinal absorption and renal retention of calcium.

The findings of present study demonstrates that serum calcium levels were significantly lower in neonates with birth asphyxia (7.73 ± 0.46 mg/dL) as compared to those without birth asphyxia (9.38 ± 0.38 mg/dL), with p value <0.001. This is in agreement with Rai *et al.*[12] who also reported significantly lower serum calcium in asphyxiated neonates (8.31 ± 0.48 mg/dL) compared to controls (9.47 ± 0.49 mg/dL; p<0.001), and with Singh *et al.*[13] who found total serum calcium at birth to be 8.04 ± 0.89 mg/dL in cases versus 9.32 ± 0.72 mg/dL in controls. The slight difference in absolute calcium values across these studies may be attributed to variation in timing of sample collection, gestational age criteria, and study population characteristics. Hassan *et al.*[14] similarly reported mean serum calcium of 7.64 ± 0.59 mg/dL among asphyxiated neonates, which is quite comparable to the values observed in present study, further supporting that

hypocalcaemia is a consistent metabolic complication of birth asphyxia. The scientific basis for this finding lies in the fact that hypoxia leads to impaired parathyroid hormone secretion, elevated calcitonin levels, and intracellular shift of calcium due to metabolic acidosis, which collectively reduces the circulating serum calcium concentration.

Ugowe *et al.*[15] reported prevalence of hypocalcaemia as 44 (43.1%) in asphyxiated neonates versus 16 (15.7%) in controls (p=0.001), and Aikta *et al.*[16] documented hypocalcaemia in 46 (22.2%) of 207 asphyxiated neonates. The comparatively higher proportion in Ugowe *et al.*[15] could be explained by larger sample size and use of a cut-off based prevalence definition rather than mean comparison. Nasrin *et al.*[17] also confirmed significantly lower calcium levels in asphyxiated neonates (p=0.001), which is consistent with the present study findings.

Regarding gender distribution, present study found equal proportion of male neonates in both groups 15 (65.2%) in each. Hassan *et al.*[14] also reported male predominance at 60% among asphyxiated neonates. However, Nasrin *et al.*[17] found no significant difference in gender distribution between groups (p=0.76), which is similar to present study where gender proportion was identical, suggesting that gender by itself does not influence the likelihood of birth asphyxia but male predominance may reflect the general tendency of male neonates being more frequently admitted in neonatal units. In present study, LSCS was the most common mode of delivery in case group 13 (56.5%) which is comparable to Aikta *et al.*[16] who reported caesarean section in 121 (58.5%) of asphyxiated neonates. This similarity suggest that operative deliveries, particularly emergency LSCS, may be associated with conditions that predispose to asphyxia such as foetal distress, cord complications, or prolonged labour, though the mode itself may sometimes be a consequence rather than a cause of asphyxia.

Regarding maternal calcium supplementation, only 7 (30.4%) mothers in case group had received supplements compared to 20 (87.0%) in control group. This finding was not specifically addressed in most of the compared studies, which represent a gap in existing literature. However, it is scientifically plausible that inadequate maternal calcium intake during pregnancy reduces placental transfer of calcium to the foetus, thereby making the neonate more susceptible to hypocalcaemia, particularly when additional metabolic stress such as birth asphyxia is superimposed. Patel *et al.*[18] and Vamne *et al.*[19] highlighted that severity of hypocalcaemia correlates with severity of asphyxia and that renal dysfunction secondary to hypoxia further impairs vitamin D activation, reducing intestinal and renal calcium absorption, which supports the multifactorial aetiology of hypocalcaemia observed in present study.

There are some limitations with the current study that should be mentioned. Firstly, it was a single-center study carried out in one hospital that might affect the generalization of the study results to a larger group. Secondly, the sample used for the study was relatively small; there were 23 neonates in each group. Moreover, serum calcium was estimated once at a certain point of time, but no serial measurements were performed.

CONCLUSION

From the current study, it can be established that the serum level of calcium in neonates who suffer from birth asphyxia is relatively lower compared to those who do not have birth asphyxia. In other words, it can be said that hypocalcemia is one of the common complications associated with birth asphyxia. Furthermore, mode of delivery and inadequate maternal calcium intake may cause hypocalcemia in neonates.

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