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ASSOCIATION OF LOW SERUM CALCIUM AND MAGNESIUM LEVELS IN TERM NEONATES WITH BIRTH ASPHYXIA

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Abstract

Objective:
To find out the association between low serum calcium and magnesium levels and birth asphyxia in term neonates.

Study Design:
Case-control study.

Place and Duration of Study:
Department of Pediatric Medicine, Services Hospital, Lahore, over a period of six months (15-11-2024 to 14-05-2025).

Patients and Methods:
A total of 180 neonates (90 cases with birth asphyxia and 90 controls without birth asphyxia) were enrolled after meeting inclusion criteria. All neonates were selected from the neonatal intensive care unit over a six-month period using a consecutive sampling technique. Blood samples were collected via venipuncture under aseptic conditions to assess serum calcium and magnesium levels. Hypocalcemia was defined as serum calcium <2 mmol/L, and hypomagnesemia as serum magnesium <1.5 mg/dL. Data was analyzed using SPSS version 25, and statistical significance was set at $p<0.05$ for all comparisons.

Results:
The mean age of the neonates was 3.37±1.67 hours, mean birth weight was 2.90±0.43 kg, and mean gestational age was 39.14±1.34 weeks. Males constituted 57.2% of the cohort, indicating a slight male predominance. Hypocalcemia was observed in 64.4% of cases versus 13.3% of controls [OR=11.78 (5.59–24.82)], showing a strong association with birth asphyxia. Hypomagnesemia was detected in 53.3% of cases compared to 12.2% of controls [OR=8.21 (3.86–17.45)], further supporting a statistically significant link between electrolyte disturbances and asphyxia.

Conclusion:
Low serum calcium and magnesium levels are significantly associated with birth asphyxia in term neonates, highlighting the importance of early electrolyte assessment in affected infants. Routine screening for these deficiencies could aid in prompt management and potentially improve neurological outcomes in this vulnerable population. Further large-scale studies are recommended to look into the underlying mechanisms and the potential role of supplementation in reducing morbidity.

INTRODUCTION:

Birth asphyxia refers to the hypoxia, hypercapnia, and acidosis that result in systemic abnormalities in neonates, including electrolyte imbalances.[1] It is a common and serious neonatal health problem, significantly contributing to neonatal morbidity and mortality.[2] Birth asphyxia is the failure to initiate and keep up breathing at birth as defined by World Health Organization (WHO) .[3] [4] It affects approximately 0.5% to 2% of live births,[5] with reported frequencies ranging from 1 to 8 per 1,000 live births in different studies.[1] [5] Among those affected, 15–25% of neonates may die during the neonatal period, while up to 25% of survivors suffer from long-term neurological complications.[6] [7]

The severity of birth asphyxia during the first and fifth minutes of life is commonly assessed using the Apgar score, which ranges from 0 to 10.[8] Birth asphyxia leads to hypoxic-ischemic tissue injury and metabolic disturbances, including significant electrolyte imbalances, which further contribute to perinatal morbidity and mortality.[9] [10] Hypocalcemia is one such metabolic derangement associated with poor prognosis in affected neonates.[11] Therefore, recognizing and understanding these electrolyte imbalances is crucial, as they have a profound impact on neonatal outcomes.[1]

Assessing and managing the electrolyte status in neonates is a critical but challenging task, as significant fluid and electrolyte shifts occur during the transition from fetal to neonatal life.[2] Magnesium, in particular, has been shown to have neuroprotective properties against hypoxic injury by supporting neuronal health. Research suggests that magnesium acts as a major NMDA receptor antagonist in the brain, helping to block excitotoxic pathways, protect cell membranes, and ultimately preserve neural function.[12] Conversely, hypomagnesemia may exacerbate neuronal injury, similar to the neurotoxic effects observed with elevated bilirubin levels. However, limited studies have investigated the incidence of decreased serum electrolytes specifically among neonates with birth asphyxia.[13]

The intention of the present study was to determine whether low serum electrolyte levels are associated with neonatal birth asphyxia. Although existing literature suggests a significant association between low serum electrolyte levels and birth asphyxia, neonates are not routinely screened for these imbalances in clinical practice. Furthermore, no prior studies have been conducted in the local healthcare setting to explore this relationship. Thus, there was a pressing need to conduct research within the local population to generate evidence that could inform clinical practice, guide maternal healthcare improvements during pregnancy, and ultimately prevent birth asphyxia. The study findings are expected to contribute to the existing literature and help refine neonatal care practices in the local context.

METHODOLOGY

This case-control study was done in the Department of Pediatric Medicine at Services Hospital, Lahore, over a period of six months, from November 15, 2024, to May 14, 2025. Preceding initiation, the study was reviewed and approved by the Institutional Review Board (IRB) of Services Hospital. Legal and ethical approvals were obtained in compliance with national and international research standards. All procedures including human participants were aligned with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its amendments or comparable ethical standards done later.

Neonates aged between 1 to 6 hours, of both genders, were considered for inclusion. Birth asphyxia was characterized as an Apgar score of less than 7 at 5 minutes on clinical examination. Patients who fulfilled the inclusion criteria were enrolled after obtaining informed consent from their parents or legal guardians. Demographic data were recorded, and Apgar scores were noted. Blood samples were gathered and sent to the hospital laboratory for evaluation of serum calcium and magnesium levels.

Electrolytes were assessed with a specific focus on hypocalcemia and hypomagnesemia.

Neonates with serum calcium levels below 2 mmol/L were categorized as hypocalcemic, and those with serum magnesium levels less than 1.5 mg/dL were categorized as hypomagnesemic.

The sample size was calculated using OpenEpi software. Based on previous research indicating hypocalcemia prevalence rates of 43.1% in cases and 15.7% in controls, and setting the study power at 80%, a total sample size of 180 neonates was determined. This included 90 cases (neonates with diagnosed birth asphyxia) and 90 controls (neonates without birth asphyxia). A non-probability convenience sampling technique was employed for enrollment.

Exclusion criteria included preterm neonates (gestational age <32 weeks as per the mother's antenatal records), neonates whose mothers had been taking calcium or magnesium supplements during pregnancy, neonates with clinical evidence of congenital diseases, those with very low birth weight (<1.5 kg), neonates with neonatal jaundice (total bilirubin >5 IU), and cases with incomplete medical records.

Data was analyzed using SPSS version 25.0. Continuous variables, namely age, birth weight, gestational age, duration of labor, Apgar score, and serum electrolyte levels, were summarized as mean ± standard deviation (SD). Categorical variables, like gender, maternal folic acid supplementation, labor duration, place of delivery, meconium staining, mode of delivery, and the presence of electrolyte abnormalities, were presented as frequencies and percentages. The odds ratio (OR) was measured to assess the association between abnormal electrolyte levels and birth asphyxia, with OR > 1 considered statistically significant.

RESULTS:

In the case group, the mean age of neonates was 3.59 ± 1.76 hours, compared to 3.14 ± 1.56 hours in the control group, with no statistically significant difference (p = 0.075). Male neonates constituted 56.7% (n=51) of the case group and 57.8% (n=52) of the control group [OR = 0.96 (95% CI: 0.53–1.72)], indicating no significant gender-related difference.

The mean birth weight was evidently lower in the case group (2.67 ± 0.33 kg) when compared to the control group (3.13 ± 0.38 kg) (p < 0.001). Similarly, the mean gestational age was slightly lower among cases (38.98 ± 1.37 weeks) than controls (39.39 ± 1.30 weeks), though this difference was not statistically significant (p = 0.108).

Maternal history of folic acid supplementation was reported in 38.9% (n=35) of the case group versus 47.8% (n=43) in the control group [OR = 0.69 (95% CI: 0.38–1.25)]. Induced labor was observed in 18.9% (n=17) of cases compared to 14.4% (n=13) of controls [OR = 1.38 (95% CI: 0.62–3.04)]. Meconium-stained amniotic fluid was found in 16.7% (n=15) of the case group and 13.3% (n=12) of the control group [OR = 1.30 (95% CI: 0.57–2.95)].

The mean duration of labor was significantly longer among mothers in the case group (11.10 ± 4.82 hours) compared to the control group (9.78 ± 3.97 hours) (p = 0.046). Cesarean section deliveries occurred in 26.7% (n=24) of cases and 22.2% (n=20) of controls [OR = 1.27 (95% CI: 0.64–2.52)].

Significantly, the mean Apgar score at five minutes was evidently lower in the case group (5.57 ± 0.92) compared to the control group (7.00 ± 1.41) (p < 0.001) **(Table I).**

Table I: Distribution of demographics of neonates enrolled in both groups (n = 180)

	Study Groups		Total
	Case	Control	
n	90	90	180
Age (in hours)	3.59 ± 1.76	3.14 ± 1.56	3.37±1.67

Gender	Male	51(56.7%)	52(57.8%)	103(57.2%)
	Female	39(43.3%)	38(42.2%)	77(42.8%)
Gestational age (weeks)		38.98 ± 1.37	39.30 ± 1.30	39.14±1.34
Birth Weight (Kg)		2.67 ± 0.33	3.13 ± 0.38	2.90±0.43

Maternal history of folic acid	Yes	35(38.9%)	43(47.8%)	78(43.3%)
	No	55(61.1%)	47(52.2%)	102(56.7%)
Induced Labor	Yes	17(18.9%)	13(14.4%)	30(16.7%)
	No	73(81.1%)	77(85.6%)	150(83.3%)
Delivery at	Clinic	42(46.7%)	41(45.6%)	83(46.1%)
	Hospital	48(53.3%)	49(54.4%)	97(53.9%)
Duration of labor		11.10 ± 4.82	9.78 ± 3.97	10.44±4.45
Meconium staining	Yes	15(16.7%)	12(13.3%)	27(15.0%)
	No	75(83.3%)	78(86.7%)	153(85.0%)
Mode of delivery	CS	24(26.7%)	20(22.2%)	44(24.4%)
	Vaginal	66(73.3%)	70(77.8%)	136(75.6%)
APGAR score		5.57 ± 0.92	7.00 ± 1.41	6.28 ± 1.39

In the case group, low calcium levels were detected in 58 (64.4%) neonates, compared to 12 (13.3%) in the control group [OR=11.78 (5.59–24.82)]. Furthermore, another assessment identified low calcium levels in 48 (53.3%) neonates in the case group and 11 (12.2%) in the control group [OR=8.21 (3.86–17.45)] **(Table II).**

Table II: Association of abnormal electrolytes level with birth asphyxia (n = 180)

		Study Groups		p-value	OR (95% CI)
		Case	Control		
n		90	90		
Serum calcium level		1.75 ± 0.34	2.28 ± 0.35	<0.001	
Low level of calcium	Yes	58(64.4%)	12(13.3%)	<0.001	11.78 (5.59-24.82)
	No	32(35.6%)	78(86.7%)		
Serum magnesium level		1.46 ± 0.28	1.99 ± 0.36	<0.001	
Low level of magnesium	Yes	48(53.3%)	11(12.2%)	<0.001	8.21 (3.86-17.45)
	No	42(46.7%)	79(87.8%)		

A bar graph was also plotted to show the distribution of serum calcium level in case and control groups (figure I).

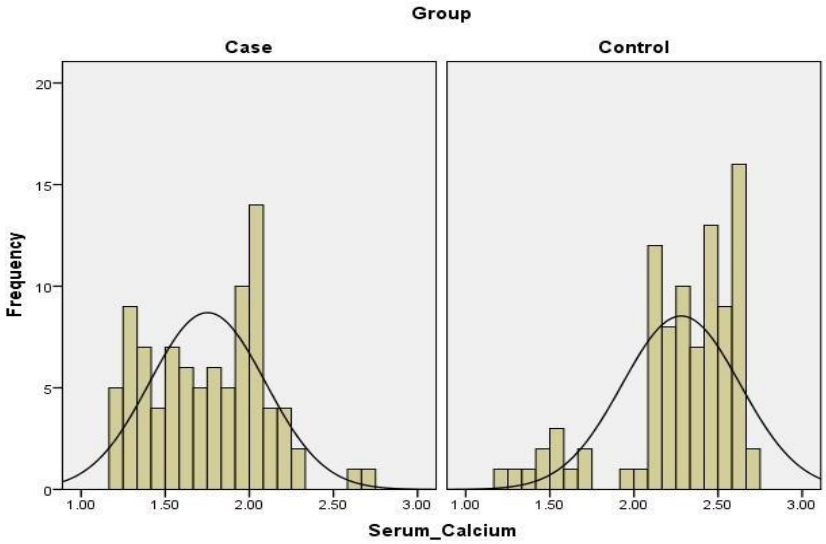

Fig I: Diagram showing distribution of serum calcium level in both groups

DISCUSSION:

Birth asphyxia is a critical condition in neonatology, characterized by oxygen deprivation leading to fetal hypoxia and hypercapnia. A hallmark of this condition is fetal acidosis, commonly defined by an umbilical cord pH of less than 7.0, typically arising during the first
or second stages of labor. Prenatal asphyxia remains a major cause of neonatal mortality, explaining approximately 20% of neonatal deaths worldwide.[15]

Similar to the findings of our study, Ugowe et al. reported significantly lower serum total calcium levels in asphyxiated neonates (43.1%) compared to controls (15.7%) (p=0.001), with an odds ratio (OR) of 4.1 (95% CI: 2.1–7.9).[14] Furthermore, the same study found that hypomagnesemia was significantly more prevalent among asphyxiated neonates (35.3%) than healthy controls (13.7%) (p=0.001; OR=3.4; 95% CI: 1.7–6.9). These findings reinforce the significant association between electrolyte imbalances—particularly hypocalcemia and hypomagnesemia—and birth asphyxia.

Magnesium, an essential intracellular electrolyte, plays a crucial role in neuromuscular function and cellular metabolism, yet remains underrepresented in neonatal research. Approximately 65% of body magnesium is stored in bones, 34% in intracellular compartments, and only 1% in extracellular fluids, with one-third of plasma magnesium bound to proteins.[16]

Ilves et al. evaluated ionized calcium and total magnesium count in neonates with hypoxic-ischemic encephalopathy (HIE). They found that neonates with mild HIE had elevated total magnesium levels compared to controls, whereas those with severe HIE exhibited lower magnesium levels ($p<0.05$), highlighting magnesium's potential role in neuroprotection.[17]

In another study by Hossain et al., fifty neonates with HIE were studied, revealing lower mean serum magnesium levels (1.6 ± 0.3 mg/dl) compared to controls (1.8 ± 0.4 mg/dl). Magnesium supplementation improved short-term neurological outcomes, suggesting therapeutic potential in neonatal asphyxia management.[18]

Similarly, Nasrin Khalessi et al. established an evident difference in blood magnesium levels between asphyxiated and non-asphyxiated neonates (p=0.01), with hypomagnesemia emerging as a significant correlate of neonatal hypoxia (OR=2.188, 95% CI: 1.826–2.626).[19]

Shamsuzzaman Prodhan et al. further supported the notion that electrolyte disturbances, including hyponatremia, hyperkalemia, and elevated serum creatinine and blood urea levels, were commonly associated with the severity of perinatal asphyxia.[20]

Contrastingly, Saha et al. reported lower mean serum magnesium levels in asphyxiated neonates (1.83 ± 0.04 mg/dl) compared to controls (1.96 ± 0.05 mg/dl). Hypomagnesemia was present in 10% of cases but absent in controls. Interestingly, while hypoglycemia was noted in 23.3% of cases, mean blood glucose levels were paradoxically higher in the case group, though not statistically significant.[21]

Given the variations observed across different studies, including discrepancies with some of our findings, it is recommended that future research involve larger, multicenter samples to validate and strengthen these associations. This would help in developing standardized protocols for the management of birth asphyxia, potentially incorporating early screening and correction of calcium and magnesium imbalances to improve neonatal outcomes.

CONCLUSION:

Our study shows a significant connection between low serum calcium and magnesium levels and the occurrence of birth asphyxia in term neonates. These findings suggest that early assessment and correction of electrolyte imbalances may play a significant role in the management and prognosis of asphyxiated newborns. Incorporating routine screening of calcium and magnesium levels in neonates at risk of asphyxia could aid in timely interventions, potentially improving short- and long-term outcomes. Further multicenter
researches with comparatively larger sample sizes are recommended to confirm these findings and guide the development of standardized management protocols.

CONFLICT OF INTEREST: None

DISCLOSURE: None

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PATIENT CONSENT: Consent from all patients was taken to use their data for research purposes

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