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ORIGINAL ARTICLE

FREQUENCY OF HYPOCALCEMIA IN NEONATES WITH PERINATAL ASPHYXIA

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Abstract

Background: Asphyxia in a basic term used when birth occurs and newborn's spontaneous respiration is delayed after delivery. More specifically, hypoxia, hypercapnia, and acidosis that cause systemic problems in the infant is known as birth asphyxia. Because of the possible consequences of hypocalcaemia, the relationship between it and fetal hypoxia is a crucial factor to take into account.

Objective: To determine the frequency of hypocalcaemia in neonates with perinatal asphyxia

Material and Methods: This cross-sectional study was conducted at the Department of Pediatric Medicine, Khalifa Gul Nawaz Teaching Hospital, Bannu, from July to December 2025. All newborns of both genders with perinatal asphyxia were included. Excluded were infants with sepsis, inborn metabolic errors, Rh incompatibility, and clinical suspicion of hematological conditions. SPSS version 25.0 was used for statistical analysis. p value <0.05 were considered statistically significant.

Results: In this study, the average gestational age was 38.03 ± 1.06 weeks. Of the 100 patients, 40 (40.0%) were male and 60 (60.0%) were female, with a male to female ratio of 1:1.5. The average weight in our sample was 3.09 ± 1.53 kg. The average serum calcium level was 2.14 ± 0.18 mg/dl. Hypocalcaemia was found in 27 (27.0%) newborns with perinatal asphyxia in our study.

Conclusion: According to our research, newborns that suffer from birth asphyxia go on to develop hypocalcaemia. When a newborn experiences hypoxia, prompt detection and effective treatment of hypocalcaemia lowers the chance of death and removes detrimental effects on neurological development.

Keywords: birth asphyxia, calcium, hypocalcaemia

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Introduction:

Asphyxia in a basic term birth occurs when a newborn's spontaneous respiration is delayed after delivery.[1] More specifically, hypoxia, hypercapnia, and acidosis that cause systemic problems in the infant is known as birth asphyxia.[2]The following criteria must be satisfied in order to diagnose asphyxia, according to the American Academy of Pediatrics (AAP) and the American College of Obstetrics and Gynecology (ACOG): severe metabolic or mixed academia (pH <7) in the cord; multiple organ involvement (kidney, lungs, liver, heart, and gut); persistence of APGAR scores 0–3 for longer than five minutes; and infant neurological Sequelae (seizures, coma, or hypotonia).[3] It is a common problem, with an incidence ranging from 0.5 to 2% of live infants. The incidence, according to some, varies between 1 and 8 per 1000 live births.[4] Hematologic illnesses, metabolic disorders such as hyponatremia and hypocalcaemia, lung diseases, gastrointestinal disorders, cerebral palsy, cardiac dysfunction, renal dysfunction, and pulmonary diseases are all consequences of prenatal hypoxia. In term neonates, hypocalcaemia is defined as a total blood calcium level of less than 2.0 mmol/L (8 mg/dL), and in preterm neonates, less than 1.75 mmol/L (7

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mg/dL).[5] Both the albumin-bound fraction and the ionized, active calcium fraction are included in the total calcium level measurement. Blood pH, serum phosphorous, serum magnesium, and albumin level all have an impact on the ionized calcium level.[6] The most typical symptom of hypocalcaemia is increased neuromuscular irritability, or jitteriness and muscle jerking brought on by background noise or other stimuli, even though the majority of infants with this condition are asymptomatic. Lethargy, distension of the abdomen, vomiting, wheezing, and focal or widespread clonic seizures are other symptoms.7Diagnosing hypocalcaemia is challenging since its symptoms are nonspecific and can be confused with those of other neonatal diseases, including as anoxic brain injury, opiate withdrawal syndrome, septicemia, hypoglycemia, and hypomagnesaemia.[8] According to a study, 21.1% of infants with prenatal asphyxia had hypocalcemia.[9]

Because of the possible consequences of hypocalcaemia, the relationship between it and fetal hypoxia is a crucial factor to take into account. In order to underline this factor and help adjust local tactics and research goals, this study aims to address the burden of hypocalcaemia in newborns with prenatal asphyxia. Since there hasn't been much research done on this topic in the past, I've chosen to carry out this investigation to find out how often hypocalcaemia is in newborns who experience prenatal hypoxia. Additionally, in order to lower the morbidity and mortality of neonates with prenatal asphyxia, this study will assist us in developing our standard practice recommendations for the early detection and treatment of hypocalcaemia.

Material and Method:

Study design: Descriptive cross-sectional study

Setting and duration: : Department of Pediatric Medicine, Bannu Medical College/Khalifa Gul Nawaz Teaching Hospital, Bannu, from July to December 2025, with ethical review committee clearance.

Sample size: The percentage of hypocalcaemia in newborns with perinatal asphyxia was determined to be 21.1%9 using the WHO calculator for single proportion, which yielded a sample size of 100 with a 95% confidence level and an 8% margin of error.

Inclusion criteria: In the study, newborn babies were approached after delivery/admission with parental informed consent. All newborns of both genders with perinatal asphyxia (APGAR score and ≤7 at 1 minute) and gestational age >28 weeks (as determined by LMP) were included.

Exclusion criteria: Excluded were infants with sepsis, inborn metabolic errors, jaundice neonatorum, or Rh incompatibility, as well as multiple pregnancies (as determined by USG), in-utero deaths (as determined by USG), and clinical suspicion of hematological conditions such as hypersplenism, leukemia, and thrombotic thrombocytopenic purpura.

Data collection procedure: he parents of each newborn gave their informed consent. Meconium-stained liquid (yes/no), low birth weight (yes/no), anemia (yes/no), gestational age, gender, neonatal weight, and delivery method (SVD/Cesarean) were then recorded. To determine the serum calcium level, a 4cc venous blood sample was sent to the lab. Hypocalcaemia was defined as serum calcium levels for term neonates of less than 2.0 mmol/L (8 mg/dL) and preterm neonates of less than 1.75 mmol/L (7 mg/dL). Every newborn was cared for in accordance with ward protocol. A pre-made proforma was used to record all of this information.

Data analysis: SPSS version 25.0 was used for statistical analysis. Serum calcium levels, neonatal weight, and gestational age were reported as mean and SD or median (IQR). Frequencies and percentages were shown for gender, mode of delivery (SVD/Cesarean), protracted rupture of membrane (yes/no), anemia (yes/no), me conium-stained liquid (yes/no), and hypocalcaemia (present/absent). Stratification was used to adjust for effect modifiers such as gestational age, gender, neonatal weight, mode of birth (SVD/Cesarean), protracted rupture of membrane (yes/no), anemia (yes/no), and me conium-stained fluid (yes/no). To determine their impact on hypocalcaemia, the post-stratification chi square/fisher exact test was used. A P-value of less than 0.05 was deemed significant.

Results:

In this study, the average gestational age was 38.03 ± 1.06 weeks. Of the 100 patients, 40 (40.0%) were men and 60 (60.0%) were women, with a male to female ratio of 1:1.5. The distribution of patients with confounding variables is shown in Table 1. The average weight in our sample was 3.09 ± 1.53 kg. The average serum calcium level was 2.14 ± 0.18 mg/dl Table 2.

Hypocalcaemia was found in 27 (27.0%) newborns with perinatal asphyxia in our study (Figure I). The stratification of hypocalcaemia according to effect modifiers is shown in Table 3.

Binary logistic regression was carried out to examine the effects of the predictors that cause hypocalcaemia. The dependent variable was Hypocalcaemia (present=1, absent=0), and odds ratios (OR) with 95% confidence intervals (CI) were determined. Regression analysis revealed that the relationship between each of the tested variables and hypocalcaemia in the neonates with perinatal asphyxia is statistically non-significant (p>0.05). Nevertheless, long-term rupture of membrane also had increased odds of being infected with hypocalcaemia (OR=1.78; 95% CI: 0.62-5.14), but this was not significant.

Table 1: Distribution of different variables (n=100)

		Frequency	%age
Gestational age (weeks)	<37	23	23.0
	≥37	77	77.0
Gender	Male	40	40.0
	Female	60	60.0
Weight (kg)	≤3	47	47.0
	>3	53	53.0
Mode of delivery	SVD	63	63.0
	Cesarean	37	37.0
Prolonged rupture of membrane	Yes	19	19.0
	No	81	81.0
Anemia	Yes	17	17.0
	No	83	83.0
Meconium-stained liquor	Yes	16	16.0
	No	84	84.0

Table 2: Descriptive statistics

	Mean	SD
Gestational age (weeks)	38.03	1.56
Weight (kg)	3.09	1.53
Serum calcium levels (mg/dl)	2.14	0.18

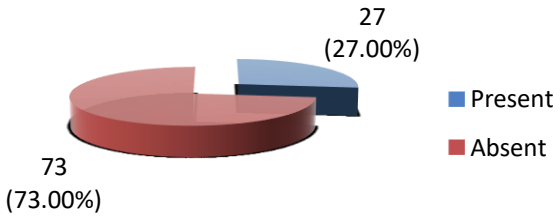

Figure I: Frequency of hypocalcaemia in neonates with perinatal asphyxia (n=100).

Table 3: Stratification of hypocalcaemia with respect to effect modifiers.

		Yes (n=27)	No (n=73)	P-value
Gestational age (weeks)	<37	06 (26.09%)	17 (73.91%)	0.911
	≥37	21 (27.27%)	56 (72.73%)	
Gender	Male	12 (30.0%)	28 (70.0%)	0.581
	Female	15 (25.0%)	45 (75.0%)	
Weight (kg)	≤3	11 (23.40%)	36 (76.60%)	0.446
	>3	16 (30.19%)	37 (69.81%)	
Mode of delivery	SVD	17 (26.98%)	46 (73.02%)	0.996
	Cesarean	10 (27.03%)	27 (72.97%)	
Prolonged rupture of membrane	Yes	07 (36.84%)	12 (63.16%)	0.283
	No	20 (24.69%)	61 (75.31%)	
Anemia	Yes	03 (17.65%)	14 (82.35%)	0.340
	No	24 (28.92%)	59 (71.08%)	
Meconium-stained liquor	Yes	05 (31.25%)	11 (68.75%)	0.676
	No	22 (26.19%)	62 (73.81%)	

Chi square test was used for p value calculation.

Table 4: Unavailable binary logistic regression analysis of predictors associated with hypocalcaemia.

Predictor	Category	OR	95% CI	P-value
Gestational age	<37 weeks vs >=37 weeks	0.94	0.33-2.71	0.911
Gender	Male vs female	1.29	0.53-3.14	0.582
Weight	<=3 kg vs >3 kg	0.71	0.29-1.73	0.447
Mode of delivery	Cesarean vs SVD	1.00	0.40-2.50	0.996
Prolonged rupture of membrane	Yes vs no	1.78	0.62-5.14	0.287
Anemia	Yes vs no	0.53	0.14-2.00	0.346
Me conium-stained liquor	Yes vs no	1.28	0.40-4.10	0.677

Discussion:

One of the body's key second messengers is calcium. It is essential for healthy muscle function and serves as a cofactor for a number of enzyme processes. Neonatal with birth asphyxia are known to experience hypocalcaemia more frequently, which can have harmful effects such as compromising cardiovascular function or causing seizures.[10] There are two types of calcium in serum: ionic calcium and total serum calcium. When serum albumin concentration is low, there is little correlation between ionized and total serum calcium levels. The three most common causes of neonatal deaths are birth asphyxia, preterm, and systemic infections.[11] Asphyxiated newborns have been seen to exhibit a variety of metabolic abnormalities. The biochemical anomalies linked to poor outcomes in birth asphyxia include hypoglycemia, hypokalemia, hyponatremia, hyperuricaemia, hypocalcaemia, and elevated createnine levels.[12]

The purpose of this study is to ascertain the prevalence of hypocalcaemia in newborns who have experienced perinatal hypoxia. 77% of the newborns in my study were term, and the mean gestational age was 38.03 ± 1.06 weeks. This is consistent with research by Lahari *et al.*[13] and Jahan *let al.*[14], who found that term neonates accounted for the majority of birth asphyxia cases. 60% of the newborns in our study were female, and this group had the highest incidence rate of birth asphyxia. Males made up 74% of participants in a study by Bahatkar and Aundhakar8 and 70% of participants in another study by Patidar *et al.*[15] In this instance, the male preponderance is explained by temporary cerebral anoxia and a

decrease in brainstem neurons involved in respiratory regulation.

Poor physiological reserves and underdeveloped organ systems have been linked to lower birth weight as a risk factor for birth asphyxia.[16] Studies like Islam A *et al*[17] which showed a higher prevalence of birth asphyxia in neonates with lower birth weights, confirm these conclusions.

Hypocalcaemia was found in 27 (27.0%) newborns with perinatal hypoxia in our investigation. According to a study, 21.1% of infants with prenatal asphyxia had hypocalcemia.[9]Hypocalcaemia was found in 43.1% of asphyxiated term infants and hypomagnesaemia in 34.3%, according to a Bangladeshi study.[18]

Kayoed et al.[19] reported a prevalence of 28.4% among all newborns with birth asphyxia. Additionally, Anolue *et al.* observed that 16.1% of healthy and unwell infants in Port Harcourt had early onset hypocalcaemia.[20] 44 (43.1%) of the 102 asphyxiated newborns in the study exhibited low serum total calcium with an OR of 4.1 compared to 16 (15.7%) of the control neonates. As the degree of birth asphyxia increased, so did the percentage of infants with hypocalcaemia (LR=10.341; p=0.035). Babies with mild, moderate, and severe birth asphyxia had median (IQR) blood total calcium levels of 2.2 (1.8-2.3) mmol/L, 1.9 (1.8-2.3) mmol/L, and 1.9 (1.7-2.4) mmol/L, respectively (H=.7.184; p =0.028).[21]

112 (54.1%) of the 207 neonates in a cross-sectional study were male. The average gestational age was 37.7 ± 0.9 weeks, and the average postnatal age was 16.6±8.4 hours. In 121 (58.5%) of the instances, the birth method was cesarean section. 36 (17.4%) and 46 (22.2%) newborns with birth asphyxia had hypomagnesaemia and hypocalcaemia, respectively.[22]

The frequency of hypocalcaemia in newborns suffering from acute hypoxia was examined in a 2011 study conducted in Nigeria.19 The study assessed total calcium levels and classified the degree of hypoxia using the Apgar score. While the asphyxiated neonates with normal calcium levels at 12 and 24 hours of life continued to have normal serum levels after 48 hours of life, the overall frequency of hypocalcaemia among the severely asphyxiated neonates was 22.6%. This study found that 57.1% of the asphyxiated newborns experienced convulsions, however not all of them had hypocalcaemia. It was unclear how many of the neonates experienced convulsions due to encephalopathy and how many were caused by hypocalcemia.[19]

Similar findings to the current study were also observed by another investigation by Njie AE*et al.* (p-value <0.05).[18] Improda *et al.* found that asphyxiated newborns had a highly substantial decrease in extracellular Ca concentration, which was closely correlated with the degree of asphyxia.[23] comparable to that reported by Bhoye et al., who found that asphyxiated newborns had a higher decrease in serum concentrations of both total and ionized calcium than non-asphyxiated neonates.[24] PA is a complete problem that causes morbidity and mortality. PA-related perinatal and neonatal mortality reveals a society's social, educational, and economic values. Asphyxia is more common in underdeveloped countries, like Pakistan, where health facilities are confined to urban areas; yet, despite the lack of local data, the topic has been thoroughly examined and thoroughly explored.

Limitations:

There were a couple of limitations in this study. Originally, it was carried out in one tertiary care hospital, thus the results might not be completely generalizable to another hospital or to the community. Second, the sample size used was relatively small, consisting of 100 neonates, which could have restricted the potential to establish statistically significant relationships between hypocalcaemia and potential predictive variables. Third, the research adopted cross-sectional design thus it was able to establish the prevalence of hypocalcaemia but failed to achieve the causal relationship between perinatal asphyxia and hypocalcaemia. Fourth, the serum calcium was only determined using a single point, and, they were not evaluated in serial calcium levels to determine any changes with time elapsing. Finally, there was no follow-up of long-term neonatal outcomes such as neurological development, seizures, morbidity, and mortality.

Future Directions:

To enhance the generalizability of results, future investigations are advised to be performed on a sizeable sample and within several centers. To ascertain the temporal association of perinatal asphyxia with hypocalcaemia development, prospective cohort studies should be carried out. Serial monitoring of serum calcium in the initial few days of life should also be incorporated in future studies to establish the trend and duration of hypocalcaemia. Also, research is needed to determine the correlation between hypocalcaemia and the grade of asphyxia at birth, stage of hypoxic-ischemic encephalopathy, seizures, necessity of entering a NICU, mortality, and neurodevelopment outcomes in the long term. Other biochemical abnormalities disruptions like those of magnesium, glucose, sodium and potassium could also be investigated further as the proponent of calcium imbalance.

Conclusion:

This study found that hypocalcaemia was present in 27% of neonates with perinatal asphyxia, indicating that low serum calcium is a common metabolic abnormality in this group. Though a slight increased prevalence of hypocalcaemia was reported in neonates when their membranes were ruptured longer, when they weighed more at birth, were male, delivered

via cesarean section or the me conium-stained liquor, none of the mentioned was significantly correlated to hypocalcaemia. Thus, screening of serum calcium levels should be done routinely in all neonates with perinatal asphyxia, irrespective of the clinical and demographic factors. By detecting and promptly treating hypocalcaemia, the timing of such complications as seizures, cardiac impairment, and negative neurodevelopment results can be minimized.

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