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Original Research Article

A study on Serum Calcium Levels Correlation with Severity of Neonates with Hypoxic Ischemic Encephalopathy

Prabhat Ranjan[1], Rajnish Mishra[2]

[1]Senior Resident, Department of Paediatrics, Jan Nayak Karpoori Thakur Medical College & Hospital, Madhepura, Bihar, India

[2]Associate Professor, Department of Paediatrics, Jan Nayak Karpoori Thakur Medical College & Hospital, Madhepura, Bihar, India

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Corresponding Author: Dr. Prabhat Ranjan

Conflict of interest: Nil

Abstract:

Objectives: Perinatal asphyxia is a leading cause of neonatal morbidity and mortality. It is defined as a condition resulting from impaired gas exchange during labor and delivery, leading to fetal hypoxemia, hypercarbia, and metabolic acidosis. The present study was to correlate the serum calcium levels with severity of neonates with Hypoxic Ischemic Encephalopathy.

Methods: Babies were divided in to two groups. Group A mild grade birth asphyxia corresponding to stage 1 sarnat and sarnat staging and group B moderate to severe birth asphyxia corresponding to grade 2 and 3 of sarnat and sarnat staging of hypoxic ischemic encephalopathy. Laboratory investigations were done including hemoglobin, total count, Differential count, serum sodium potassium and calcium. Serum total calcium was estimated in auto-analyzer.

Results: Mean weight of the babies in study was 2.34 ± 0.61 kg. Out of total 95 birth asphyxia babies, hypocalcemia was present in 32(33.68%) neonates. Out 70 neonates of group A, 20(28.57%) neonates had hypocalcemia. Similarly, out of 25 neonates of group B, 12(48%) neonates had hypocalcemia. It was not statistically significant differenced (p=0.813). One (5%) neonate was expired among 20 mild HIE hypocalcemic neonates of group A. similarly among 12 hypocalcemic neonates of group B, 5 neonates (41.675%) were expired. Out of 32 hypocalmic neonates, 6(18.75%) neonates were expired.

Conclusions: Hypocalcaemia is very common in HIE neonates. Mortality rate is greater in moderate to severe HIE neonates as compared to mild HIE hypo calcaemic neonates.

Keywords: Birth asphyxia, Hypoxic Ischemic Encephalopathy, Hypocalcemia.

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Introduction

Perinatal asphyxia is a leading cause of neonatal morbidity and mortality. It is defined as a condition resulting from impaired gas exchange during labor and delivery, leading to fetal hypoxemia, hypercarbia, and metabolic acidosis [1].

Globally, hypoxia of the newborn is estimated to account for 23% of the 4 million neonatal deaths each year [2]. An estimated 1 million children who survive from birth asphyxia live with chronic neurodevelopmental morbidities, including cerebral palsy, mental retardation, and learning disabilities. Perinatal asphyxia is defined by the World Health Organization (WHO) as the failure to initiate and sustain breathing at birth. The WHO definition of birth asphyxia in the International Classification of Diseases (ICD-10) is based on the Apgar scoring system. An Apgar score at 1 min of 0-3 defines severe birth asphyxia and an Apgar score of 4-7 defines mild and moderate birth asphyxia [3].

Severe cases may progress to hypoxic ischemic encephalopathy (HIE), a serious neurological sequela associated with long-term neurodevelopmental impairment and significant socioeconomic burden [4]. Birth asphyxia is frequently associated with multiple metabolic derangements, including hypoglycemia, hypocalcemia, hyponatremia, hyperphosphatemia, and metabolic acidosis [5].

Calcium is an essential element involved in numerous physiological processes, including neuromuscular function and enzymatic activity. During fetal life, calcium is actively transported across the placenta, resulting in higher fetal calcium levels compared to maternal levels [6]. After birth, the sudden cessation of placental calcium transfer

leads to a transient decline in serum calcium levels [7]. In neonates with perinatal asphyxia, this physiological adaptation may be disrupted, increasing the risk of hypocalcemia, which can contribute to neuromuscular irritability and seizures [8].

Hypocalcemia occurs with increased frequency in neonates with birth asphyxia [9]. Hypocalcemia in asphyxiated infants may trigger seizures or may compromise cardiovascular function with deleterious consequences [10]. The present study was to correlate the serum calcium levels with severity of neonates with Hypoxic Ischemic Encephalopathy.

Material & Methods

The present study was conducted in the Department of Pediatrics, Jan Nayak Karpoori Thakur Medical College & Hospital, Madhepura, Bihar, India during a period from September 2025 to January 2026.

Inclusion Criteria: Babies with APGAR score of less than 7 at 5 minute and only in born babies were included in the study.

Exclusion Criteria: Babies with congenital cardio pulmonary malformation, those born mother with diabetes mellitus and hypertension treated with diuretics, general anaesthesia, phenobarbitone, pethidine, magnesium sulphate and other drugs likely to cause depression.

Methods

Hypocalcemia is defined as total serum calcium of less than 7 mg/dL (1.75 mmol/L) or ionized calcium less than 4 mg/dL (1 mmol/L) in preterm infants and less than 8 mg/dL (2 mmol/L; total) or <1.2 mmol/L (ionic) in term neonates. Babies were divided in to two groups. Group A mild grade birth asphyxia corresponding to stage 1 sarnat and sarnat staging and group B moderate to severe birth asphyxia corresponding to grade 2 and 3 of sarnat and sarnat staging of hypoxic ischemic encephalopathy.

Cases were selected based on inclusion criteria and detailed clinical examination was done and physical findings were recorded on pre designed proforma. Blood sample was collected and following investigations were done hemoglobin, total count. Differential count, serum sodium potassium and calcium. Serum total calcium was estimated in auto-analyzer.

Statistical Analysis: Data was analysed with the help of SPSS version 26 software. Mean and standard deviation were observed. Chi-squared test was applied. P-value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Results

A total of 95 neonates had birth asphyxia were enrolled in the study. Group A had 70 babies mild birth asphyxia and in Group B had 25 babies moderate to severe birth asphyxia. Out of 95 babies, 54 were male and 41 were female. Mean weight of the babies in study was 2.34 ± 0.61 kg.

Table 1: Showing the HIE neonates.

Group	Staging HIE	Number of cases (N=95)	Serum calcium levels (Mean ± S.D.)	P-value
Group A	Mild	70(73.68%)	6.98 ±1.98	
Group B	Moderate to Severe	25(26.32%	7.05 ±2.0	0.808

Out of 95 birth asphyxia babies, hypocalcemia was present in 32(33.68%) neonates. Out 70 neonates of group A, 20 (28.57%) neonates had hypocalcemia. Similarly, out of 25 neonates of group B, 12(48%) neonates had hypocalcemia. It was not statistically significant differenced (p=0.813).

Table 2: Showing the hypocalcemia in HIE neonates.

Group	Hypocalcemia	Serum calcium levels (Mean ± S.D.)	P-value
Group A (Mild HIE) (N=70)	20(28.57%)	5.82±0.91	
Group B (Moderate to severe HIE (N=25)	12(48%)	5.78±1.38	0.813

One (5%) neonate was expired among 20 mild HIE hypocalcemic neonates of group A. similarly among 12 hypocalcemic neonates of group B, 5 neonates (41.675%) were expired. Out of 32 hypocalmic neonates, 6(18.75%) neonates were expired.

Table 3: Showing the mortality in hypocalcemic neonates.

Group	Hypocalcemia	Deaths in hypocalcemia
Group A (Mild HIE)	20	1(5%)
Group B (Moderate to severe HIE)	12	5(41.67%_
Total	32	6(18.75%)

Discussions

Birth asphyxia is one of the leading causes of neonatal morbidity and mortality, particularly in low- and middle income countries. It results from a lack of oxygen (hypoxia) and/or inadequate blood flow (ischemia) to the foetus or newborn during the perinatal period. This critical condition can lead to multi-organ dysfunction and has profound effects on the neonatal metabolic profile, including disturbances in electrolyte levels such as calcium. The evaluation of calcium homeostasis, especially both total serum calcium and ionized calcium, is essential in understanding the biochemical consequences of birth asphyxia and guiding appropriate clinical interventions [11]. Neonatal hypocalcemia is a common biochemical abnormality observed in asphyxiated neonates. It can occur early (within the first 72 hours) or late (after 72 hours) and often presents without specific clinical symptoms, making routine biochemical monitoring indispensable. Calcium plays a vital role in cellular signaling, muscle contraction, neurotransmitter release, and cardiac rhythm regulation. The two primary components of serum calcium include total calcium, which comprises both bound and unbound fractions, and ionized calcium, which is the biologically active and physiologically significant component. Of the total calcium present in serum, approximately 50% exists in the ionized form, 40% is protein-bound (mostly to albumin), and the remaining 10% is complexed with anions [12]. Birth asphyxia leads to a cascade of metabolic derangements, including hypoxia-induced acidosis and disturbances in parathyroid hormone function, which are implicated in the pathogenesis of hypocalcemia. The hypoxic state impairs calcium mobilization from bones and reduces intestinal calcium absorption, while also causing an increase in phosphate levels that further suppress calcium concentrations. Moreover, the stress response to asphyxia, accompanied by elevated catecholamines and glucocorticoids, contributes to altered calcium metabolism. These changes are more effectively reflected by measuring ionized calcium levels, which are more sensitive to acute physiological variations than total serum calcium [13]. Clinical and biochemical profiling of neonates with birth asphyxia has shown significant derangements in electrolytes, particularly calcium and glucose levels. Early identification and correction of these abnormalities are critical to improving outcomes in affected neonates. Studies have suggested that hypocalcemia in birth asphyxia may worsen the neurological status by exacerbating seizure activity and contributing to cardiac dysfunction [14].

In the present study hypocalcemia was present in 32(33.68%) cases of total 95 hypoxic ischemic encephalopathic cases. In Onyiriuka study, the overall prevalence (22.6%) of early-onset neonatal hypocalcaemia in birth asphyxia cases [15]. Behrman et al, in 1974 in USA compared the serum calcium levels of 42 neonates with birth asphyxia with 42 control neonates, matched for gestational age and sex. Neonates with asphyxia had lower serum calcium levels at 12 and 24 hours of life [16]. Petersen et al. (1981), described hypocalcemia in asphyxiated infants with more severe degrees of asphyxia [17]. Jajoo et al showed a significant low serum calcium levels in asphyxiated babies than controls [10].

In the present study moderate to severe HIE cases with hypocalcemia had more mortality rate (41.67%) than compared to mild cases of HIE (5%).

Lila A et al, study concluded that significant correlation between severity of HIE and decreased serum levels ionized calcium, significant relation between decreased serum levels ionized calcium decreased survival rate [18].

Numerous metabolic derangements exist in asphyxiated newborns such as hypoglycemia, hypocalcemia, hypomagnesemia, etc. [19,21]. In the present study, the levels of calcium in the blood were decreased in newborns who had birth asphyxia. These results are consistent with Manzke and Kruse [20] who concluded that both the total and ionized calcium levels in asphyxiated newborns were decreased as compared to the ones who were born healthy.

Jajoo et al. [10] studied the impact of serum calcium and phosphorus on asphyxiated newborns. Serial measurements of these electrolytes in the blood from birth till the fifth day of life revealed that babies born with birth asphyxia had low levels of calcium and phosphorous.

Conclusions

The present study concluded that the hypocalcaemia is very common in HIE neonates. Mortality rate is greater in moderate to severe HIE neonates as compared to mild HIE hypo calcaemic neonates.

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