

EPIDEMIOLOGY OF HYPOCALCAEMIA IN NICU OF A TEACHING HOSPITAL OF EASTERN REGION OF INDIA

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Abstract

Background: Neonatal hypocalcemia is a common yet challenging anomaly, often asymptomatic and transient, posing potential threats to newborns. The absence of a well-established definition and controversy surrounding therapeutic cutoff levels add complexity to clinical assessment. This study aims to explore the epidemiology of hypocalcemia in a NICU setting in Eastern India, investigating prevalence, associated risk factors. **Materials and Methods:** A cross-sectional study was conducted at an eastern Indian teaching hospital's NICU from July 2020 to June 2021. Participants included newborns aged <28 days admitted specifically for hypocalcemia or those developing it during NICU stay. Exclusions comprised major congenital anomalies, out-born newborns, and those without parental consent. Hypocalcemia definitions varied based on birth weight, and data were collected through venous samples and detailed documentation. **Result:** Out of 628 deliveries, 14 newborns (2.23%) developed hypocalcemia, with a prevalence of 16.28% in NICU admissions. Males outnumbered females (5:2), and the term-to-preterm ratio was 1:1. Common delivery mode was Lower Uterine Caesarean Section (LUCS) (78.58%). Hypocalcemia was prevalent in newborns with a birth weight ≥ 2500 g (50%). Early onset neonatal hypocalcemia (EONH) occurred in 6 cases, while 8 developed late-onset neonatal hypocalcemia (LONH). Respiratory distress (50%) and jaundice (50%) were predominant symptoms, and Pregnancy-Induced Hypertension (PIH) emerged as a common precipitating factor (37.5%). **Conclusion:** The study highlights a 16.28% prevalence of hypocalcemia in NICU, predominantly affecting males and newborns with a birth weight ≥ 2500 g. PIH and birth asphyxia emerged as significant risk factors, with a noteworthy proportion of asymptomatic cases. Respiratory distress was the leading associated pathology. Further multicenter, long-term studies are warranted to comprehensively explore the epidemiological profile and trends. Limitation of this study is single-centered with a short span in a NICU setting, emphasizing the need for extensive, multicenter, and longitudinal investigations from both NICU and OPD settings.

INTRODUCTION

Hypocalcemia, a prevalent laboratory and clinical anomaly during the neonatal period, poses potential threats to newborns. Despite its common occurrence, neonatal hypocalcemia is often asymptomatic and transient, making its diagnosis and management challenging. Furthermore, the absence of a well-established definition for hypocalcemia in the

neonatal population, along with controversy surrounding the therapeutic cutoff levels of low serum calcium, adds complexity to its clinical assessment.^[1]

For term infants or preterm infants with a birth weight exceeding 1500 g, hypocalcemia is confirmed when the total serum calcium falls below 8 mg/dL (2 mmol/L) or an ionized fraction drops below 4.4 mg/dL (1.1 mmol/L).^[2] In very low birth weight (VLBW) preterm infants (BW < 1500 g),

hypocalcemia is diagnosed when the total serum calcium is less than 7 mg/dL (1.75 mmol/L) or the ionized fraction is below 4 mg/dL (1 mmol/L).^[3,4]

Hypocalcemia is further classified into early onset neonatal hypocalcemia (EONH) and late onset neonatal hypocalcemia (LONH), based on the time of onset. EONH, occurring within the first 72 hours, is commonly observed in neonates with intrauterine growth restriction, birth asphyxia, prematurity and infants born to diabetic mothers. On the other hand, LONH, manifesting beyond 72 hours, is associated with factors such as vitamin D deficiency, cow milk intake, and hypo-parathyroidism.^[5]

Clinical manifestations of hypocalcemia in neonates vary, with the less mature infants displaying subtle signs. Key clinical indicators include jitteriness (increased neuromuscular irritability) and generalized convulsions. Additionally, nonspecific symptoms such as poor sucking, vomiting, somnolence, lethargy, poor feeding, and abdominal distention may be present.^[6,7]

Despite the potential severity of neonatal hypocalcemia, there is a noticeable lack of information regarding its epidemiology in India. This study aims to investigate the epidemiological profile of neonates with hypocalcemia, identify associated risk factors, and formulate preventive and therapeutic strategies tailored to the unique characteristics of this setting.

MATERIALS AND METHODS

Study Design and Setting: This research employed a cross-sectional study design conducted at the Neonatal Intensive Care Unit (NICU) of an eastern Indian teaching hospital. The study spanned from July 2020 to June 2021, following the receipt of ethical clearance from the institute.

Participants: The study included all newborns aged less than 28 days admitted to the NICU specifically for hypocalcemia or those who developed hypocalcemia during their NICU stay. Newborns with major congenital anomalies, out-born newborn and those whose parents did not provide consent were excluded from participation.

Definition of Hypocalcemia: For term infants or preterm infants with a birth weight exceeding 1500 g, hypocalcemia was defined as a total serum calcium

level falling below 8 mg/dL (2 mmol/L) or an ionized fraction dropping below 4.4 mg/dL (1.1 mmol/L). In very low birth weight (VLBW) preterm infants (BW < 1500 g), hypocalcemia was diagnosed when the total serum calcium was less than 7 mg/dL (1.75 mmol/L) or the ionized fraction was below 4 mg/dL (1 mmol/L).^[2-4]

Data Collection: Venous samples (1 ml) were collected at 24 hours and 72 hours of life for serum calcium level from all high-risk newborns i.e. newborn with prematurity, birth asphyxia, maternal history of diabetes, and intake of anti-epileptic drugs. Serum calcium levels were measured for all sick newborns admitted to NICU and repeated at 48-hour intervals. For cases of late-onset neonatal hypocalcemia (LONH), additional tests including serum PTH, creatinine, magnesium, and Vitamin D were performed. Both asymptomatic and symptomatic newborns were managed according to standard protocols.^[5,8]

All data, including detailed history, examination findings, and laboratory reports, were recorded in a data collection form.

Data Analysis: Statistical analysis was conducted using SPSS software version 19.0 for Windows. Descriptive statistics were applied on the above dataset.

RESULTS

Out of 628 deliveries, 14 newborn developed hypocalcemia. Prevalence came out to be 2.23%. Out of 86 NICU admission 16.28% (14) babies have developed hypocalcemia. Male: female ratio was 5:2. Ratio of term baby to preterm baby is 1:1. Table 1 depicts LUCS is common mode of delivery in cases of hypocalcemia. [Table 2] Distribution of birth weight among neonates with hypocalcemia.

[Table 2] depicts hypocalcemia is common in newborn with birth weight \geq 2500gm EONH was found in 6 cases whereas 8 neonates developed LONH. [Table 4] depicted respiratory distress is the most common symptoms. [Table 5] depicts PIH is most commonly associated with hypocalcemia. Table 6 depicts half of the cases of hypocalcemia did not receive phototherapy. Only in 1 case phototherapy started before diagnosis of hypocalcemia.

Table 1: Distribution of mode of delivery among neonates with hypocalcemia

Mode of delivery	N	Percentage
Lower uterine cesarean section (LUCS)	11	78.58
Normal vaginal delivery (NVD)	3	21.42

Table 2: Birth weight and hypocalcemia

Body weight	N	Percentage
ELBW weight < 1000 gm	1	7.14%
VLBW-weight 1000-1499 gm	4	28.57%
LBW-weight 1500-2499 gm	2	14.29%
Body weight 2500 gm or more	7	50%

Table 3: Distribution of term and preterm baby in EONH and LONH

Gestational age	EONH	LONH
Term	4	3
Preterm	2	5
Total	6	8

Table 4: Distribution of symptom in hypocalcaemic neonates

Symptoms	N	Percentage
Respiratory distress	7	50%
Abdominal distention, feed intolerance	4	28.57%
Jitteriness	2	14.28%
Seizure	1	7.14%
Asymptomatic	3	21.43%
Jaundice	7	50%

Table 5: Distribution of precipitating factors in hypocalcaemic neonates

Precipitating factor	N	Percentage
Pregnancy induced hypertension (PIH)	3	37.5%
Birth asphyxia	2	25%
Gestational Diabetes Mellitus (GDM)	1	12.5%
Prolonged rupture of membrane (PROM)	1	12.5%
Meconium stained liquor (MSL)	1	12.5%

Table 6: Distribution of phototherapy in hypocalcaemic neonates

Phototherapy	N	Percentage
DSPT-Double surface photo therapy	6	42.86
SSPT-Single surface photo therapy	1	7.14
No phototherapy	7	50%

DISCUSSION

In our study, we observed that 16.28% of neonates admitted to the Neonatal Intensive Care Unit (NICU) exhibited hypocalcaemia, with a prevalence of 2.23% among all live births. These figures, while lower than those reported by Raguž MJ, Bošnjak I,^[9] are consistent with the findings of Ayash FF et al. from Jordan.^[10] Notably, Kushal Aggarwal et al. reported a significantly higher prevalence of neonatal hypocalcaemia (76%) in a sample of 100 neonates in an outpatient department (OPD)-based study conducted in the western part of India.^[11]

Our research aligns with previous studies indicating a male preponderance in hypocalcaemia, consistent with the findings of Qahtan Khayoon Hammod Alyasiri and Bhavya SO et al.^[12,13]

In our study term preterm ratio is 1:1. This is in agreement with other study.^[6,12] Khalesi et al in their study found high percentage of premature neonate developed hypocalcaemia.^[14] Routine prophylaxis calcium therapy might be responsible for less incidence of hypocalcaemia in pre term baby. Among the hypocalcaemic newborn, born by LUCS is most common. High incidence LUCS may attribute to it. This is also in agreement with other study.^[14]

Our study indicates a higher incidence of hypocalcaemia in newborns with a birth weight of 2500 grams or more, in line with findings from other studies.^[6,12] As for associated symptoms/pathologies, respiratory distress and jaundice were the most common, followed by abdominal distention and vomiting. A noteworthy observation was that 21% of cases were asymptomatic, consistent with the study by Raguž MJ, Bošnjak I,^[6] but differing from the

findings in the study by Qahtan Khayoon Hammod Alyasiri from Iraq.^[12]

We have found PIH is the most common precipitating factor followed by birth asphyxia. Nasrin Khalesi et al found positive association between low apgar at 1 minute and GDM with onset of hypocalcaemia.^[12] Ratio of newborn with hypocalcaemia received phototherapy to non receiver was 1:1. Basnet S et al found a negative but insignificant correlation between the duration of phototherapy and hypocalcaemia in term neonates.^[15]

CONCLUSION

In summary, our research sheds light on the prevalence and characteristics of neonatal hypocalcaemia among NICU-admitted neonates. Prevalence of hypocalcaemia in NICU is 16.28% with male preponderance. Prematurity and low birth weight did not stand as a potential risk factor for hypocalcaemia compared to term and normal weight baby. PIH and birth asphyxia are risk factor for development of hypocalcaemia. A good number of patients may be totally asymptomatic. Respiratory distress was the most common associated pathology.

Limitation: It is a single centered study with short span in a NICU setting. Multi centered long term study from NICU and OPD require to explore full epidemiological profile and trend.

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