e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(4); 578-582

Original Research Article

Risk Factors for Hypocalcemia in Preterm Neonates: A Prospective Observational Study

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Received: 01-01-2026 / Revised: 15-02-2026 / Accepted: 21-03-2026

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Conflict of interest: Nil

Abstract

Background: Neonatal hypocalcemia is a frequent metabolic abnormality, particularly in preterm infants, and is associated with significant morbidity. Early identification of risk factors is essential for timely intervention.

Aim: To determine the prevalence and evaluate maternal and neonatal risk factors associated with hypocalcemia in preterm neonates.

Methods: This prospective observational study was conducted in a tertiary care neonatal intensive care unit and included 100 preterm neonates. Relevant maternal and neonatal clinical data were collected. Biochemical parameters including serum calcium, magnesium, phosphorus, vitamin D, and parathyroid hormone levels were measured. Statistical analysis was performed using appropriate tests, and a p-value <0.05 was considered statistically significant.

Results: The prevalence of hypocalcemia was 38%. Lower gestational age was significantly associated with hypocalcemia (p<0.001). Maternal factors such as gestational diabetes mellitus (p<0.001), preeclampsia (p=0.001), and vitamin D deficiency (p<0.001) showed strong associations. Among neonatal factors, respiratory distress syndrome was significantly associated (p<0.001). Antenatal steroid administration demonstrated a protective effect (p<0.05). Biochemical analysis revealed significantly lower parathyroid hormone levels in affected neonates.

Conclusion: Hypocalcemia is a common metabolic disturbance in preterm neonates and is influenced by multiple maternal and neonatal factors. Early screening and targeted preventive strategies are essential to improve neonatal outcomes.

Keywords: Hypocalcemia, Preterm Neonates, Gestational Age, Vitamin D Deficiency, Neonatal Risk Factors.

DOI: 10.25258/ijcpr.18.4.96

Introduction

Calcium is an essential mineral involved in neuromuscular activity, enzymatic reactions, and intracellular signaling [1,4]. In neonates, calcium homeostasis undergoes significant physiological adaptation after birth. Preterm infants are particularly vulnerable to disturbances in calcium metabolism due to immature endocrine regulation, reduced calcium stores [2,8], and associated clinical conditions.

Hypocalcemia in neonates is commonly classified as early or late onset, with early-onset hypocalcemia typically occurring within the first 72 hours of life [1,3]. Although it may remain asymptomatic in many cases, it can present with serious manifestations such as seizures, apnea, or cardiac dysfunction [3,4]. Multiple maternal and neonatal factors have been implicated in the development of hypocalcemia. Maternal conditions such as gestational diabetes mellitus and preeclampsia may impair calcium transfer and Neonatal adaptation [1,10] and hormonal regulation. Additionally, maternal vitamin D deficiency has emerged as a significant and potentially modifiable risk factor [5,6,7]. Neonatal conditions such as respiratory distress syndrome further contribute to metabolic instability [8]. Despite existing knowledge, the relative contribution of these risk factors varies across populations. Therefore, this study was conducted to determine the prevalence and identify the key risk factors associated with hypocalcemia in preterm neonates.

Materials and Methods

Study Design and Setting: This prospective observational study was conducted in the neonatal intensive care unit of a tertiary care hospital.

Study Population: A total of 100 preterm neonates (gestational age <37 weeks) admitted during the study period were included.

Inclusion Criteria:

- Preterm neonates (<37 weeks gestation)

Exclusion Criteria:

- Major congenital anomalies
- Severe perinatal asphyxia
- Incomplete clinical data

Data Collection: Maternal and neonatal clinical details were recorded using a structured proforma. Maternal variables included gestational diabetes mellitus, preeclampsia, and vitamin D status. Neonatal variables included gestational age, birth weight, and presence of respiratory distress syndrome.

Biochemical Analysis: Blood samples were collected and analyzed for serum calcium, magnesium, phosphorus, vitamin D, and parathyroid hormone levels using standard laboratory methods.

Definition: Hypocalcemia was defined based on standard neonatal reference values for serum calcium.

Statistical Analysis: Data were analyzed using appropriate statistical methods. Categorical variables were compared using chi-square test, and continuous variables were analyzed using suitable parametric or non-parametric tests. A p-value <0.05 was considered statistically significant.

Results

Prevalence of Hypocalcemia: The overall prevalence of hypocalcemia among preterm neonates in this study was 38%.

Table 1: Prevalence of Hypocalcemia

Hypocalcemia Status	Frequency	Percentage
Present	38	38%
Absent	62	62%

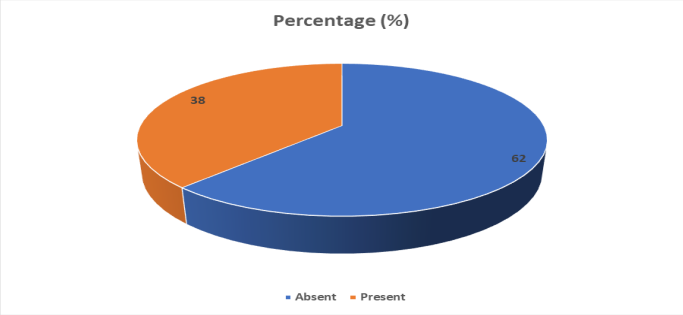

Figure 1: Prevalance of hypocalcemia

Association with Gestational Age: A statistically significant association was observed between lower gestational age and hypocalcemia (p<0.001).

Table 2: Gestational Age vs Hypocalcemia

Gestational Age	Hypocalcemia Present	Hypocalcemia Absent	p-value
28–31.6 weeks	85.7%	14.3%	<0.001*
32–37 weeks	30.2%	69.8%	

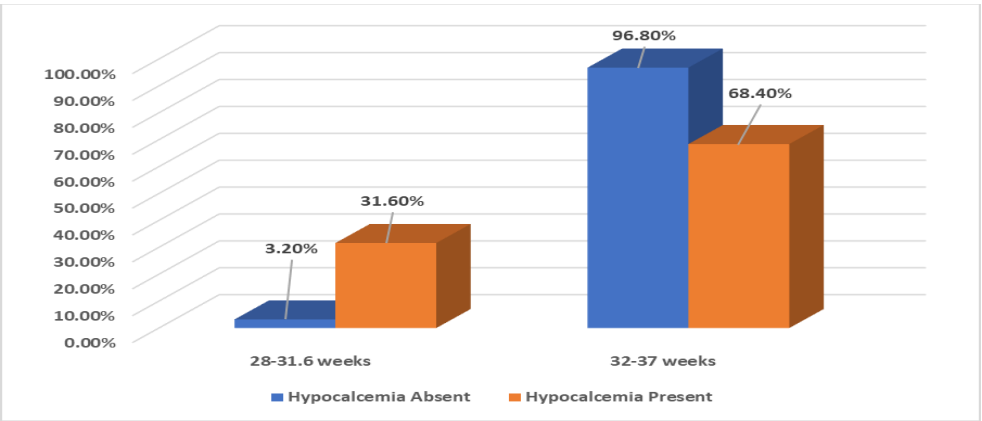

Figure 2: Gestational age and hypocalcemia

Association with Birth Weight: Lower birth weight was significantly associated with hypocalcemia (p=0.044).

Table 3: Birth Weight vs Hypocalcemia

Birth Weight	Hypocalcemia Present
≤1000 g	75%
1001–1500 g	66.7%
1501–2500 g	33.3%

Maternal Risk Factors: Maternal conditions including gestational diabetes mellitus, preeclampsia, and vitamin D deficiency showed strong associations with neonatal hypocalcemia.

Table 4: Maternal Risk Factors

Factor	Hypocalcemia Present	Hypocalcemia Absent	p-value
GDM	81.3%	29.8%	<0.001*
Preeclampsia	72.2%	30.5%	0.001*
Vitamin D Deficiency	73.1%	25.7%	<0.001*
Antenatal Steroids	15.5%	—	<0.001*

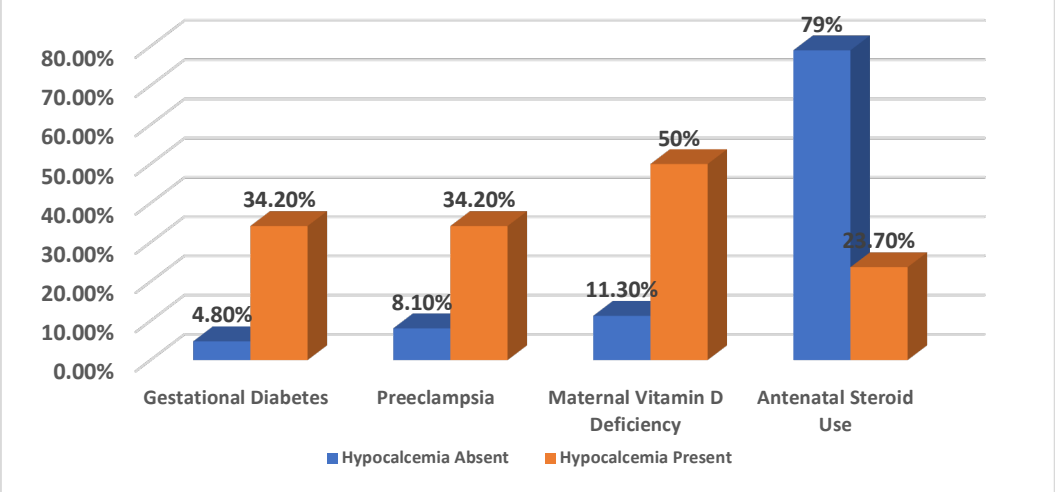

Figure 3: Maternal risk factors and hypocalcemia

Neonatal Risk Factors: Respiratory distress syndrome was significantly associated with hypocalcemia, whereas sepsis did not show statistical significance.

Table 5: Neonatal Risk Factors

Factor	Hypocalcemia Present	Hypocalcemia Absent	p-value
RDS	63.3%	27.1%	<0.001*
Sepsis	52.6%	34.6%	0.145

Biochemical Findings: Significant differences were observed in biochemical parameters between the hypocalcemia and normal groups.

Table 6: Biochemical Comparison

Parameter	Hypocalcemia	Normal	p-value
Ionized Calcium	0.96 ± 0.11	1.27 ± 0.12	<0.001*
PTH	12.60 ± 4.38	26.32 ± 7.53	<0.001*
Vitamin D	22.38 ± 10.04	28.87 ± 7.86	<0.001*
Magnesium	1.68 ± 0.43	1.87 ± 0.28	0.006*

Respiratory Distress Syndrome

Table 7: Respiratory Distress Syndrome and Hypocalcemia

RDS	Hypocalcemia Absent	Hypocalcemia Present	p-value
No	51 (82.3%)	19 (50.0%)	**<0.001***
Yes	11 (17.7%)	19 (50.0%)	
Total	**62 (100.0%)**	**38 (100.0%)**	

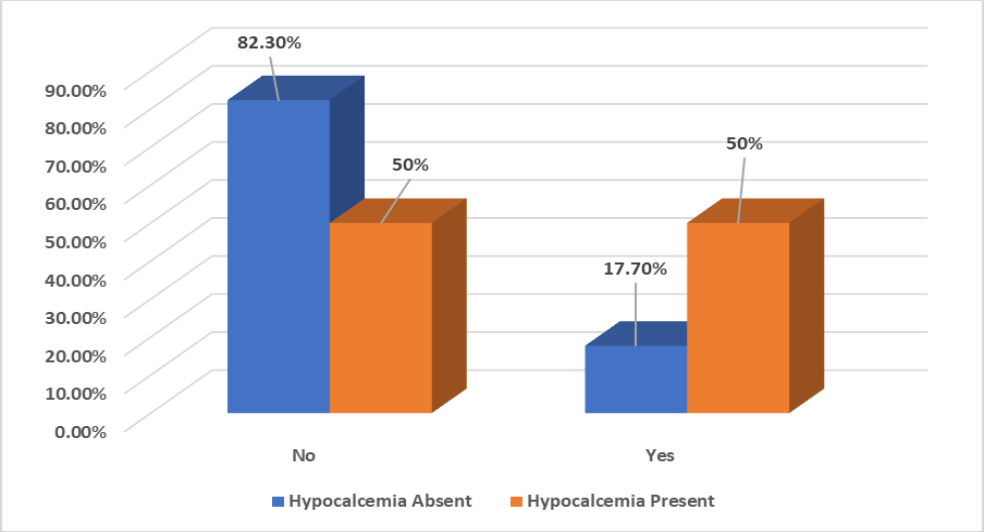

Figure 4: Respiratory Distress syndrome and Hypocalcemia

Table 7 and Figure 4 .The presence of RDS was significantly associated with hypocalcemia ($p<0.001$). This strong association highlights RDS as an important risk factor for hypocalcemia, likely related to increased metabolic demands, stress, and the pathophysiology of lung immaturity in preterm infants.

Discussion

The present study demonstrated a high prevalence of hypocalcemia (38%) among preterm neonates, emphasizing its clinical significance. Lower gestational age was identified as the strongest predictor, which can be attributed to immature parathyroid function and reduced calcium reserves [2,8].

Maternal conditions such as gestational diabetes mellitus and preeclampsia were significantly associated with neonatal hypocalcemia.

These conditions may interfere with placental calcium transport and neonatal hormonal adaptation [1,10]. Maternal vitamin D deficiency was also strongly associated, highlighting its importance as a modifiable risk factor [5,6,7].

Respiratory distress syndrome was significantly associated with hypocalcemia, possibly due to increased metabolic stress and altered calcium homeostasis [8]. Antenatal steroid administration appeared to have a protective effect, likely by enhancing neonatal physiological maturity.

The observation of reduced parathyroid hormone levels in affected neonates suggests transient functional hypoparathyroidism as a contributing mechanism [2,3].

Limitations

- **Limited sample size and statistical power:** The study included only 100 preterm neonates, which may have limited the ability to detect statistically significant associations despite clinically relevant trends.
- **Single-centre study design:** Being conducted at a single tertiary care centre, the findings may not be generalizable to other settings with different populations and clinical practices.
- **Short follow-up period:** The study evaluated only early-onset hypocalcemia without assessing long-term outcomes such as neurodevelopment, growth, or bone health.
- **Unmeasured confounders and incomplete data:** Lack of detailed maternal nutritional information and incomplete characterization of antenatal steroid exposure may have influenced the results. Additionally, serum albumin levels were not accounted for, which could have affected the interpretation of total calcium levels.

Conclusion

Hypocalcemia is a common metabolic disorder in preterm neonates and is influenced by multiple maternal and neonatal factors.

Early identification of at-risk neonates and implementation of preventive strategies are essential to reduce associated morbidity and improve outcomes.

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