International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Original Researcher Article *DOI: 10.61336/im/26-06-164*

CLINICAL PROFILE AND MATERNAL-NEONATAL RISK FACTORS ASSOCIATED WITH IONIZED HYPOCALCEMIA AMONG NEONATES ADMITTED TO A TERTIARY CARE NEONATAL INTENSIVE CARE UNIT: A PROSPECTIVE OBSERVATIONAL STUDY.

[1]Dr. A. Deva Prasanna, [2]Dr. Suresh P.M, [3]Dr. Veena R.S.

[1]Junior Resident, Department of Pediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekaram, Tamil Nadu, India

[2]Professor, Department of Pediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekaram, Tamil Nadu, India

[3]Junior Resident, Department of Pediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekaram, Tamil Nadu, India.

Correspondence:
Dr. A. Deva Prasanna.
Junior Resident, Department of Pediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekaram, Tamil Nadu, India..

Received: 10-05-2026
Revised: 23-05-2026
Accepted: 08-06-2026
Published: 25-06-2026

Abstract

Background: A common metabolic anomaly seen in neonatal intensive care units, especially in preterm and very unwell infants, is neonatal hypocalcaemia. Particularly in ill neonates, when albumin concentration and acid-base status may change total calcium readings, ionised calcium—the physiologically active portion of circulating calcium—offers a more clinically relevant evaluation of calcium status than total serum calcium. ***Objectives:*** to assess the biochemical features, clinical profile, maternal-neonatal risk factors, and short-term consequences of ionised hypocalcaemia in newborns hospitalised to a tertiary care neonatal intensive care unit.***Methods:***56 newborns with verified ionised hypocalcaemia who were admitted to a tertiary care neonatal intensive care unit over a ten-month period were included in this prospective observational study. Analysis was done on maternal risk factors, neonatal traits, clinical manifestations, biochemical parameters, onset pattern, and results. Frequencies and percentages were used to express categorical data, whereas mean ± standard deviation was used to express continuous variables. The independent t-test, chi-square test, or Fisher exact test were used for group comparisons as needed. To find independent predictors of symptomatic hypocalcaemia, multivariable logistic regression was employed. ***Results:*** A total of 56 newborns were examined. The average birth weight was 2.38 ± 0.64 kg, and the average gestational age was 35.27 ± 3.35 weeks. There were 35 (62.5) preterm newborns and 31 (55.4) low birth weight infants. Maternal connections included pregnancy-induced hypertension 13 (23.2), gestational diabetes mellitus 16 (28.6), and maternal anaemia 19 (33.9). newborn risk factors were delayed feeding 14 (25.0), birth asphyxia 18 (32.1), and newborn infection 22 (39.3). The most prevalent clinical symptom was jitteriness 25 (44.6). The average ionised calcium concentration was 0.874 ± 0.099 mmol/L. Ionised calcium levels were substantially lower in newborns with symptoms than in those without (0.828 ± 0.082 versus 0.963 ± 0.058 mmol/L; $p<0.001$). Prematurity, birth asphyxia, and male sex were independent predictors of symptomatic hypocalcaemia on adjusted analysis. ***Conclusion:*** Among neonates admitted to the NICU, ionised hypocalcaemia is a metabolic condition that is clinically significant, especially in preterm and low birth weight babies. In high-risk newborns, particularly those with prematurity, birth asphyxia, sepsis, and maternal metabolic risk factors, targeted screening utilising ionised calcium estimate should be taken into consideration.

Keywords: ionised calcium, low birth weight, prematurity, newborn sepsis, birth asphyxia, neonatal hypocalcaemia, NICU.

INTRODUCTION

One of the many metabolic problems that newborns experience is neonatal hypocalcaemia, which continues to be a significant cause of morbidity in neonates referred to neonatal intensive care units (NICUs). Neuromuscular transmission, myocardial contractility, blood coagulation, intracellular signalling, enzyme activation, and hormone production all depend on calcium. A wide range of clinical symptoms, including jitteriness, poor eating, apnoea, seizures, and cardiovascular instability, can result from a disruption in calcium homeostasis during the neonatal period. Foetal calcium concentrations are higher than maternal calcium concentrations because calcium is actively transferred across the placenta during foetal life. The third trimester is when the majority of foetal calcium accretion takes place. Because premature birth disrupts placental mineral transport, preterm neonates are more susceptible to hypocalcaemia,linked to immature parathyroid hormone response, decreased skeletal mineral storage, and immature kidneys.

Early-onset hypocalcaemia, which happens within the first 72 hours of life, and late-onset hypocalcaemia, which happens after 72 hours, are the two main categories for neonatal hypocalcaemia. Prematurity, low birth weight, newborns of diabetic mothers, birth asphyxia, and neonatal infection are all frequently linked to early-onset hypocalcaemia. High phosphate consumption, vitamin D deficiency, hypomagnesaemia, and aberrant parathyroid hormone secretion or action are more frequently linked to late-onset hypocalcaemia. Ionised calcium is the physiologically active portion of calcium, even though total blood calcium has historically been utilised for diagnosis. Serum albumin levels, pH, and other biochemical changes can impact total calcium readings in severely sick newborns. Thus, ionised calcium measurement is especially helpful in NICU settings and provides a more accurate assessment of clinically severe hypocalcaemia.

Neonatal hypocalcaemia is caused by a number of maternal and neonatal causes. Infants may be at risk for temporary functional hypoparathyroidism if their mothers have diabetes mellitus. The severity of newborn disease or foetal mineral reserves may be indirectly impacted by pregnancy-induced hypertension, maternal anaemia, and protracted rupture of membranes. Impaired calcium homeostasis has been linked to neonatal conditions such prematurity, low birth weight, birth asphyxia, sepsis, delayed feeding, and respiratory disease. There is still a dearth of Indian data explicitly addressing ionised hypocalcaemia in newborns referred to the NICU, despite its clinical significance. Determining the clinical characteristics and risk factors of ionised hypocalcaemia may aid medical professionals in creating focused screening plans and starting prompt therapy. The goal of the current investigation was to assess the clinical characteristics,

AIM

To investigate the clinical characteristics and maternal-neonatal risk factors linked to ionised hypocalcaemia in newborns admitted to a neonatal critical care unit for tertiary treatment.

OBJECTIVES

- To assess the clinical characteristics of newborns suffering from ionised hypocalcaemia.
- To determine the risk variables for newborn ionised hypocalcaemia in mothers.
- To determine the risk variables for newborn ionised hypocalcaemia.
- To contrast neonates with ionised hypocalcaemia who are symptomatic and those who are not.
- To evaluate the immediate results of ionised hypocalcaemia in newborns.

MATERIALS AND METHODS

Study design and setting

Sree Mookambika Institute of Medical Sciences' Neonatal Intensive Care Unit in Kulasekaram, Tamil Nadu, India, was the site of this prospective observational study.

Study duration and sample size

The research was carried out over a ten-month period. 56 neonates who met the eligibility requirements and had proven ionised hypocalcaemia were included.

Inclusion criteria

Included were newborns with ionised hypocalcaemia who were admitted to the NICU. Ionised calcium levels less than 1.1 mmol/L in term neonates and less than 1.0 mmol/L in preterm neonates were considered ionised hypocalcaemia.

Exclusion criteria

Neonates with insufficient clinical records, those with significant congenital defects, and those who had undergone calcium treatment prior to admission were not included.

Data collection

A structured proforma was used to gather data. Anaemia, gestational diabetes mellitus, hypertension brought on by pregnancy, exposure to prenatal steroids, and protracted rupture of membranes lasting more than eighteen hours were among the maternal factors. Sex, gestational age, birth weight, prematurity, low birth weight status, birth asphyxia, neonatal sepsis, delayed feeding, infant-of-diabetic-mother status, mode of delivery, age at detection, and onset type were among the neonatal factors.

Clinical and biochemical assessment

Jitteriness, poor eating, convulsions, irritability, and apnoea were among the clinical characteristics evaluated. Ionised calcium, total serum calcium, serum magnesium, blood glucose, and a sepsis screen were among the laboratory measures. Hypocalcaemia was classified as either early-onset (detected within 72 hours of life) or late-onset (detected after 72 hours).

Outcome assessment

Improvement and discharge, longer than seven days in the NICU, referral or discharge upon request, and mortality were among the short-term outcomes.

Statistical analysis

SPSS version 26.0 was used to analyse the data, and Python-based statistical analysis was used to confirm the results. Categorical variables were expressed as frequencies and percentages, whereas continuous variables were expressed as mean ± standard deviation. Continuous variables were compared using the independent t-test. For categorical variables based on anticipated cell counts, the chi-square test or Fisher exact test were employed. For clinically significant predictors, odds ratios with 95% confidence intervals were computed. To find independent predictors of symptomatic hypocalcaemia, multivariable logistic regression was used. Statistical significance was defined as a p-value of less than 0.05.

Ethical considerations

After receiving approval from the Sree Mookambika Institute of Medical Sciences' Institutional Ethics Committee, the study was carried out. Throughout the trial, patient data confidentiality was upheld.

RESULTS

The investigation comprised 56 infants with verified ionised hypocalcaemia.

Table 1. Baseline demographic and neonatal characteristics

Variable	Value
Total neonates	56 (100.0)
Male	33 (58.9)
Female	23 (41.1)
Gestational age, weeks	35.27 ± 3.35
Birth weight, kg	2.38 ± 0.64
Preterm	35 (62.5)
Term	21 (37.5)
Low birth weight	31 (55.4)
Normal birth weight	25 (44.6)
LSCS delivery	26 (46.4)
Vaginal delivery	30 (53.6)
Early-onset hypocalcemia (≤72 h)	38 (67.9)
Late-onset hypocalcemia (>72 h)	18 (32.1)

Table 2. Maternal risk factors

Maternal risk factor	n	%
Maternal anemia	19	33.9
Gestational diabetes mellitus	16	28.6
Pregnancy-induced hypertension	13	23.2
Antenatal steroid exposure	12	21.4
PROM >18 hours	9	16.1

Table 3. Neonatal risk factors

Neonatal risk factor	n	%
Prematurity	35	62.5
Low birth weight	31	55.4
Neonatal sepsis	22	39.3
Birth asphyxia	18	32.1
Delayed feeding	14	25.0
Infant of diabetic mother	11	19.6

Table 4. Clinical profile

Clinical variable	n	%
Symptomatic hypocalcemia	37	66.1
Asymptomatic hypocalcemia	19	33.9
Jitteriness	25	44.6
Poor feeding	20	35.7
Seizures	11	19.6
Irritability	10	17.9
Apnea	8	14.3

Table 5. Biochemical and clinical course profile

Parameter	Mean ± SD	Median	Range
Ionized calcium (mmol/L)	0.874 ± 0.099	0.890	0.68-1.06
Total serum calcium (mg/dL)	7.35 ± 0.51	7.45	6.2-8.3
Serum magnesium (mg/dL)	1.84 ± 0.28	1.80	1.4-2.3
Blood glucose (mg/dL)	78.34 ± 21.99	79.5	43-118
Age at detection (hours)	67.70 ± 47.80	56.5	6-162
NICU stay (days)	6.20 ± 4.43	5.0	2-18

Table 6. Comparison of continuous variables between symptomatic and asymptomatic neonates

Variable	Symptomatic (n=37)	Asymptomatic (n=19)	p-value
Gestational age (weeks)	34.75 ± 3.04	36.29 ± 3.75	0.131
Birth weight (kg)	2.43 ± 0.66	2.29 ± 0.62	0.467
Ionized calcium (mmol/L)	0.828 ± 0.082	0.963 ± 0.058	<0.001
Total serum calcium (mg/dL)	7.14 ± 0.46	7.75 ± 0.31	<0.001
Serum magnesium (mg/dL)	1.82 ± 0.27	1.87 ± 0.31	0.580
Blood glucose (mg/dL)	77.62 ± 20.47	79.74 ± 25.23	0.754
NICU stay (days)	6.65 ± 4.83	5.32 ± 3.48	0.242

Table 7. Comparison of categorical variables between symptomatic and asymptomatic neonates

Variable	Symptomatic (n=37)	Asymptomatic (n=19)	Fisher exact p-value
Male sex	26 (70.3)	7 (36.8)	0.023
Prematurity	28 (75.7)	7 (36.8)	0.008
Low birth weight	20 (54.1)	11 (57.9)	1.000
Maternal anemia	11 (29.7)	8 (42.1)	0.385
Gestational diabetes mellitus	12 (32.4)	4 (21.1)	0.534
Pregnancy-induced hypertension	9 (24.3)	4 (21.1)	1.000
PROM >18 hours	4 (10.8)	5 (26.3)	0.247
Neonatal sepsis	18 (48.6)	4 (21.1)	0.082
Birth asphyxia	15 (40.5)	3 (15.8)	0.076
Delayed feeding	11 (29.7)	3 (15.8)	0.338
Infant of diabetic mother	8 (21.6)	3 (15.8)	0.732
Early-onset hypocalcemia	25 (67.6)	13 (68.4)	1.000
Prolonged NICU stay >7 days	10 (27.0)	1 (5.3)	0.077

Table 8. Univariate predictors of symptomatic ionized hypocalcemia

Variable	Odds ratio	95% CI	Fisher exact p-value
Male sex	4.05	1.26-13.04	0.023
Prematurity	5.33	1.61-17.66	0.008
Neonatal sepsis	3.55	0.99-12.75	0.082
Birth asphyxia	3.64	0.90-14.70	0.076
Low birth weight	0.86	0.28-2.61	1.000
Delayed feeding	2.26	0.55-9.34	0.338
Prolonged NICU stay >7 days	6.67	0.78-56.69	0.077

Table 9. Multivariable logistic regression for symptomatic hypocalcemia

Variable	Adjusted OR	95% CI	p-value
Prematurity	16.32	2.61-102.10	0.003
Neonatal sepsis	4.22	0.88-20.25	0.072
Birth asphyxia	5.89	1.01-34.36	0.049
Male sex	7.40	1.46-37.50	0.016

Prematurity, neonatal sepsis, birth asphyxia, and male sex are among the variables that are part of the model. The updated model should be regarded as exploratory due to the small sample size.

Table 10. Short-term outcomes

Outcome	n	%
Improved and discharged	49	87.5
Referred/discharged on request	4	7.1
Prolonged NICU stay (>7 days)	11	19.6
Mortality	3	5.4

There were 33 (58.9) male neonates in the research population, indicating a male predominance. The average birth weight was 2.38 ± 0.64 kg, and the average gestational age was 35.27 ± 3.35 weeks. There were 35 (62.5) preterm neonates and 31 (55.4) low birth weight newborns. 38 (67.9) had early-onset hypocalcaemia.

With 19 cases (33.9), maternal anaemia was the most common maternal relationship. Thirteen (23.2) had pregnancy-induced hypertension, and sixteen (28.6) had gestational diabetes mellitus. Prematurity and low birth weight were the most common newborn risk factors, followed by neonatal infection and birth asphyxia.

37 (66.1) had symptomatic hypocalcaemia. The most common symptom was jitteriness, which was followed by apnoea, poor eating, convulsions, and irritability. The average ionised calcium level was 0.874 ± 0.099 mmol/L. Ionised calcium and total blood calcium levels were much lower in newborns with symptoms than in those without. Neonatal infection and birth asphyxia demonstrated clinically significant relationships with borderline Fisher exact significance, but prematurity and male sex demonstrated substantial univariate connections with symptomatic hypocalcaemia. Prematurity, birth asphyxia, and male sex continued to be independent predictors in the adjusted logistic regression model.

DISCUSSION

The clinical profile and maternal-neonatal risk factors linked to ionised hypocalcaemia in newborns admitted to a tertiary care NICU were assessed in this study. The most prevalent newborn risk factor was prematurity (62.5%), which was followed by low birth weight (55.4%). Given that a significant amount of foetal calcium accretion takes place during the third trimester of pregnancy, these findings are biologically feasible. Therefore, transplacental calcium transport is disrupted by premature birth, which lowers calcium reserves and raises the risk of hypocalcaemia. Similarly, due to insufficient mineral reserves and related neonatal diseases, low birth weight babies are more susceptible to metabolic disorders. Maternal anaemia (33.9%) and gestational diabetes mellitus (28.6%) were the most commonly found correlations among maternal risk variables. One known risk factor for newborn hypocalcaemia is maternal diabetes.

It is thought to play a role through the newborn's altered calcium regulation and temporary functional hypoparathyroidism. Maternal anaemia may increase the risk of newborn hypocalcaemia by reflecting low maternal nutritional status and reduced foetal mineral accretion. In the current investigation, birth asphyxia (32.1%) and neonatal sepsis (39.3%) were frequently linked diseases. Monitoring calcium levels in severely unwell newborns is crucial since both diseases are known to disturb calcium homeostasis through inflammatory and metabolic pathways. These results confirm that newborns with

serious perinatal and systemic diseases require greater attention. The most prevalent clinical symptom was jitteriness, which was followed by seizures and poor eating. Similar findings have been documented in earlier research, where the most common manifestation of newborn hypocalcaemia was neuromuscular irritability. The occurrence of seizures.

highlights the clinical importance of early detection and timely treatment in a significant percentage of neonates. This study's key conclusion was that newborns with symptoms had far lower ionised calcium levels than those without. Since ionised calcium is the physiologically active portion of serum calcium and has a stronger correlation with clinical symptoms than total serum calcium, this finding supports the usefulness of ionised calcium estimate. Ionised calcium is a more accurate diagnostic sign in severely unwell newborns since serum albumin levels and acid-base abnormalities might affect total calcium values. After receiving the proper care, most infants had positive results and were successfully discharged. Important strengths include the prospective study design, ionised calcium measurement, and investigation of maternal and neonatal risk variables.

CONCLUSION

Among neonates admitted to the NICU, ionised hypocalcaemia is a metabolic condition that is clinically relevant, especially in preterm and low birth weight babies. Birth asphyxia, neonatal sepsis, gestational diabetes mellitus, and maternal anaemia were frequently linked. The most common clinical symptom was jitteriness. Ionised calcium and total blood calcium levels were considerably lower in newborns with symptoms than in those without. In the adjusted model, symptomatic hypocalcaemia was independently predicted by male sex, prematurity, and birth asphyxia. Ionised calcium estimation-based targeted screening of high-risk newborns may promote early diagnosis, timely treatment, and better short-term neonatal outcomes.

REFERENCES

1. Cheng E, George AA, Bansal SK, Nicoski P, Amin S. Neonatal hypocalcemia: common, uncommon, and rare etiologies. NeoReviews. 2023;24(4):e217-e228.
2. Vuralli D. Clinical approach to hypocalcemia in newborn period and infancy: who should be treated? Int J Pediatr. 2019;2019:4318075.
3. MSD Manual Professional Edition. Neonatal hypocalcemia. Merck & Co., Inc.; updated 2024.
4. Cho WI, Yu HW, Chung HR, Shin CH, Yang SW, Choi CW, et al. Clinical and laboratory characteristics of neonatal hypocalcemia. Ann Pediatr Endocrinol Metab. 2015;20(2):86-91.
5. Tuchman S. Disorders of mineral metabolism in the newborn. Curr Pediatr Rev. 2014;10(2):133-141.
6. Hay WW Jr. Care of the infant of the diabetic mother. Curr Diab Rep. 2012;12(1):4-15.
7. Thomas TC, Smith JM, White PC, Adhikari S. Transient neonatal hypocalcemia: presentation and outcomes. Pediatrics. 2012;129(6):e1461-e1467.
8. Jain A, Agarwal R, Sankar MJ, Deorari AK, Paul VK. Hypocalcemia in the newborn. Indian J Pediatr. 2010;77(10):1123-1128.
9. Kliegman RM, St Geme JW, Blum NJ, Shah SS, Tasker RC, Wilson KM, editors. Nelson Textbook of Pediatrics. 21st ed. Philadelphia: Elsevier; 2020.
10. Cooper MS, Gittoes NJL. Diagnosis and management of hypocalcaemia. BMJ. 2008;336(7656):1298-1302.