Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/24133
DOI URL: http://dx.doi.org/10.21474/IJAR01/24133

RESEARCH ARTICLE

NEONATAL HYPOCALCEMIA AND THE MATERNAL–NEONATAL VITAMIN D AXIS: A TERTIARY NICU CROSS-SECTIONAL STUDY

Dhakchennya Sekar, Uma Muralidharan, Bharani Amala, Arun Priya KP and Kanan

Manuscript Info

Manuscript History
Received: 08 July 2026
Final Accepted: 10 August 2026
Published: September 2026

Abstract

Neonatal hypocalcemia, a frequently encountered metabolic disorder in the Neonatal Intensive Care Unit (NICU), can pose serious health risks to newborns. It is typically defined by reduced serum calcium levels, with threshold values varying based on gestational age and birth weight. In term infants and preterm neonates weighing more than 1500 g, hypocalcemia is considered when total serum calcium falls below 8 mg/dL (2 mmol/L) or ionized calcium below 4.4 mg/dL (1.1 mmol/L). In very low birth weight infants (<1500 g), lower cutoff values are used [1]. Based on time of onset, neonatal hypocalcemia is broadly categorized into Early-onset hypocalcemia (EOH) and Late-onset hypocalcemia (LOH). Early-onset hypocalcemia usually develops within the first 72 hours of life and is associated with a physiological decline in calcium levels after birth, along with a delayed parathyroid hormone response. In contrast, late-onset hypocalcemia typically presents after the initial 3 days, often toward the end of the first postnatal week, and is more likely to be symptomatic.[2]. The clinical presentation can vary widely. Some neonates may exhibit mild features such as irritability, tremors, or increased neuromuscular excitability, while others may develop more severe complications including seizures, apnea, or cardiac dysfunction [3,4]. Hence, early detection and prompt management are indispensable, as untreated neonatal hypocalcemia can adversely affect neurodevelopment and skeletal mineralization.

Introduction:-

Maternal vitamin D status has emerged as an important factor influencing neonatal calcium balance. Vitamin D facilitates calcium absorption from the gastrointestinal tract and supports maintenance of adequate circulating calcium levels. [5]. During pregnancy, sufficient maternal vitamin D is necessary to ensure effective transfer of calcium to the developing fetus. When maternal levels are inadequate, this transfer may be compromised, increasing the likelihood of hypocalcemia in the newborn [6]. This risk is particularly pronounced in preterm infants, who have a limited capacity to regulate calcium levels due to immature organ systems. The incidence of hypocalcemia is higher in preterm and low birth weight neonates, as they miss the critical period of intrauterine calcium accretion [7].

Corresponding Author:- Dhakchennya Sekar

Limited parathyroid responsiveness and reduced efficiency of calcium handling further increase their vulnerability. In addition, the early neonatal period represents a critical window for skeletal mineralization, making adequate calcium availability especially important [8]. Given the growing recognition of the role of vitamin D in neonatal health, understanding the relationship between maternal vitamin D status and neonatal calcium levels is essential. The present study was designed to determine the prevalence of neonatal hypocalcemia among NICU admissions and to examine its association with vitamin D levels in both mothers and neonates. Understanding this relationship may help guide preventive strategies, including maternal supplementation, to improve neonatal outcomes.

Materials and Methods:-

Study design: This prospective, single-centre-based cross-sectional study was conducted in the NICU of Meenakshi Mission Hospital and Research Centre. The study was conducted from February 2024 to February 2025 in neonates admitted as inpatients after obtaining a written informed consent from the parents or legal guardians. Ethical approval was obtained from the Institutional Ethics Committee (IEC), and the study was conducted in accordance with the Declaration of Helsinki.

Inclusion & Exclusion criteria:-

All inborn and outborn preterm and term neonates admitted as inpatients were included. Neonates with congenital anomalies, those without parental consent for blood investigations, and those not admitted as inpatients were excluded.

Data collection:-

The required data namely gender of the neonate, gestational age, birth weight, vitamin D status, etc., were recorded from the respective medical records. Venous blood was drawn from the neonates to measure serial serum calcium levels at day 0, day 3, and beyond day 3 as indicated. In cases of hypocalcemia, serum albumin was also assessed to exclude pseudo-hypocalcemia. Neonatal as well as maternal vitamin D levels were also measured.

Data analysis:-

The minimal sample size was calculated using the formula $N = Z^2P(1-P)/e^2$ ($Z = 1.96$ for 95% confidence interval, P = prevalence, and e = 5% precision), yielding a total of 100 neonates. However, a total of 124 eligible neonates were included during the study period. Categorical variables including gender, birth weight, gestational age, presence of hypocalcemia, and vitamin D status, were expressed as frequencies and percentages, and associations between categorical variables were assessed using Fisher's exact test. Correlations between continuous variables, including serum calcium levels and maternal and neonatal vitamin D levels, were analyzed using Pearson's correlation coefficient. Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA), and a p-value <0.05 was considered statistically significant.

Results:-

Among the 124 neonates included in the study, there was a male predominance (75, 60%) compared to females (49, 40%), and most neonates were preterm (80, 65%) and had low birth weight (78, 63%). Neonatal hypocalcemia was observed in 28 (23%) neonates, while 96 (77%) had normal calcium levels. Among those, 17 (61%) were males, and 11 (39%) were females, with a higher proportion occurring in preterm infants (18, 64%) compared to term infants (10, 36%) (Table 1).

Table 1: Baseline characteristics, prevalence, and distribution of hypocalcemia

Variable	Total (n=124)	Hypocalcemia (n=28)	EOH (n=17)	LOH (n=11)
Gender				
Male	75 (60%)	17 (61%)	11	6
Female	49 (40%)	11 (39%)	6	5

			p value - 0.701	p value - 0.673
Birth weight				
Normal	46 (37%)	—	8	2
Low birth weight	78 (63%)	—	9	9
			p value - 0.421	p value - 0.209
Gestational age				
Term	44 (35%)	10 (36%)	9	1
Preterm	80 (65%)	18 (64%)	8	10
			p value - 0.105	p value - 0.09
Calcium status				
Normal	96 (77%)	—	—	—
Hypocalcemia	28 (23%)	—	—	—

Among hypocalcemic neonates, Early-onset hypocalcemia (EOH) was more common, accounting for 17 (61%) cases, while late-onset hypocalcemia (LOH) was seen in 11 (39%). On analysis using Fisher's exact test,no statistically significant association were found between type of hypocalcemia and gender (EOH: p=0.701; LOH: p=0.673), birth weight (EOH: p=0.421; LOH: p=0.209), and gestational age (EOH: p=0.105; LOH: p=0.09), although LOH was more frequently observed in preterm and low birth weight neonates (Table 1).

A significant association between neonatal vitamin D deficiency and hypocalcemia was identified using Fisher's exact test. Among EOH cases, 10 (58.8%) neonates were vitamin D deficient (p=0.023), with 80% of the mothers also being deficient. In LOH, all neonates (100%) and their mothers were vitamin D deficient, showing a strong association with neonatal vitamin D deficiency (p=0.023) (Table 2). This strongly suggests that vitamin D deficiency, in both the neonate and the mother, is a critical and potentially obligatory factor in the development of LOH.

Correlation analysis performed using Pearson's correlation coefficient demonstrated no significant relationship between maternal vitamin D levels and neonatal calcium at Day 0 ($r = -0.07$, $p = 0.730$) and Day 3 ($r = 0.07$, $p = 0.705$). However, a strong positive correlation was observed beyond Day 3 ($r = 0.57$, $p < 0.001$) (Fig. 1) (Table 2). This indicates that higher maternal Vitamin D levels are strongly predictive of higher calcium levels in infants beyond the first three days of life, underscoring a crucial link that develops after the initial postnatal period. Among hypocalcemic neonates, a weak, non-significant positive correlation was noted between maternal and neonatal vitamin D levels ($r = 0.113$, $p = 0.566$) (Table 2).

Table 2: Association of hypocalcemia type and vitamin D status with correlation analysis

Association of hypocalcemia type and vitamin D status			
Variable	**EOH (n=17)**	**LOH (n=11)**	**p value**
Neonatal Vitamin D deficiency	10 (58.8%)	11 (100%)	0.023*

Maternal Vitamin D deficiency	80%	100%	0.055
Correlation analysis (Pearson's correlation coefficient)			
Parameter	**r value**	**p value**	
Maternal Vit D vs Calcium Day 0	-0.07	0.730	
Maternal Vit D vs Calcium <3 days	0.07	0.705	
Maternal Vit D vs Calcium >3 days	0.57	<0.001*	

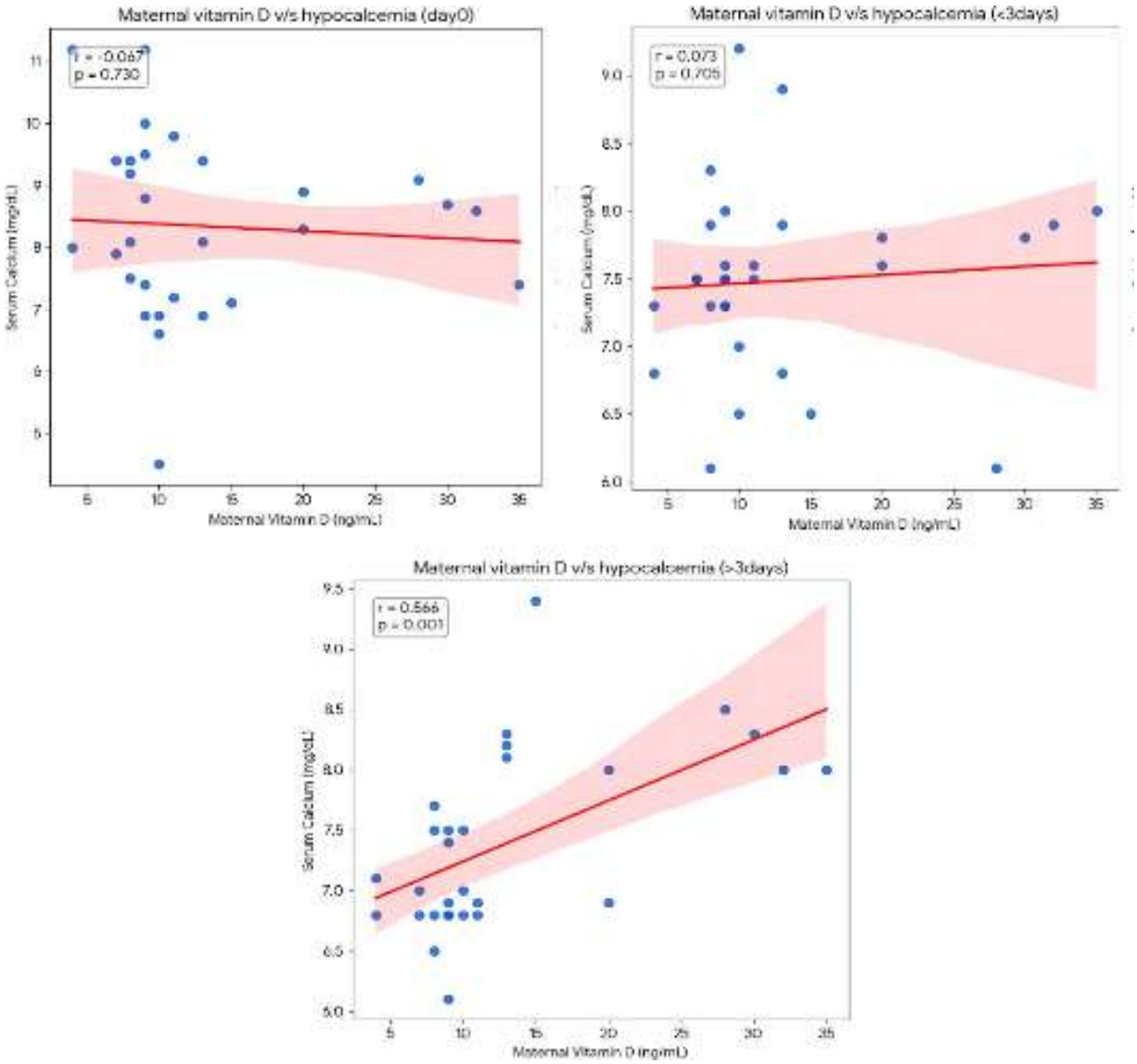

Fig.1: Scatter plots showing the correlation between maternal vitamin D levels and neonatal serum calcium levels at day 0, <3 days, and >3 days. Each point represents an individual neonate.

Discussion:-

In the present study, neonatal hypocalcemia was observed in 23% of NICU admissions, indicating a considerable burden in a tertiary care setting. This prevalence is comparable to Subendhu Saha et al., who reported 16.28% among NICU admissions and 2.23% among live births [9], and Jyoti Shrestha et al., documented 19% incidence [10]. However, wide variation exists, with Elsary et al. reporting a markedly higher incidence (76%) [11] and with Hammod Alyasiri, a lower prevalence (4.01%) restricted to symptomatic neonates [12]. Such variability reflects heterogeneity in study populations, diagnostic thresholds, and inclusion criteria. Physiologically, this burden is explained by the abrupt cessation of placental calcium transfer at birth, leading to a transient fall in serum calcium during the first 24–48 hours of life.

A male predominance was noted, with 61% of hypocalcemic neonates being male, although this difference was not statistically significant (p=0.701). Similar trends were reported by Seymen-Karabulut et al. (60.4% males) [13] and Subendhu Saha et al. (M: F ratio 5:2)[9]. These findings suggest that gender differences are likely incidental rather than causative. Prematurity emerged as a key clinical correlate, with 64% of hypocalcemic neonates being preterm. This aligns with Nabiel N et al., who reported hypocalcemia in 62.5% of preterm neonates with a significant association with vitamin D deficiency (p=0.029) [14]. Similarly, Yilmaz B et al. found that 17.2% of preterm infants developed hypocalcemia, with significantly lower vitamin D levels in affected neonates (p=0.02) [15]. These findings underscore the role of prematurity-related physiological immaturity, including reduced third-trimester calcium accretion, impaired PTH response, and decreased renal and intestinal calcium handling, as described by Vuralli et al. [8]

Early-onset hypocalcemia (EOH) was more frequent in our study, accounting for 60.7% of cases, compared to 39.3% for LOH. This is consistent with findings by Elsary et al. and Seymen-Karabulut et al.,[11,13] although Jyoti Shrestha et al. reported a higher proportion of LOH [10]. The timing difference reflects underlying pathophysiology: EOH is associated with transient hypoparathyroidism and perinatal stress, whereas LOH, typically presenting after 3–5 days, is more closely linked to nutritional factors such as vitamin D deficiency and high phosphate intake, as described by Sethi et al [16]. Birth weight also demonstrated a clinically relevant trend. Although not statistically significant across subtypes, 81.8% of LOH cases occurred in low-birth-weight infants. This finding aligns with Babu et al., who reported significantly lower gestational age and birth weight among hypocalcemic neonates ($p<0.05$). The vulnerability of low-birth-weight infants is explained by reduced intrauterine mineral accretion and immature renal calcium handling.

A major finding of this study is the strong association between vitamin D deficiency and neonatal hypocalcemia. Among EOH cases, 58.8% of neonates were vitamin D deficient (p=0.023), with 80% of their mothers also deficient. In LOH, the association was striking, with 100% (11/11) of neonates and 100% of mothers being vitamin D deficient (p=0.023). These findings are consistent with Seymen-Karabulut et al., who reported vitamin D deficiency in 86.5% of neonates and 93% of mothers, with a strong maternal–neonatal correlation ($p<0.001$) [13]. Similarly, Aasif Aziz Wani et al. demonstrated that 100% of neonates born to vitamin D-deficient mothers were hypocalcemic [17]. Correlation analysis in the present study showed no significant association between maternal vitamin D levels and neonatal calcium in the early postnatal period (Day 0: $r = -0.07$, p=0.730; Day 3: $r = 0.07$, p=0.705), but a strong positive correlation beyond Day 3 ($r = 0.57$, $p<0.001$). This reflects the transition from placental calcium supply to neonatal endocrine regulation. Similar findings were reported by Hashemipour et al. and El Koumi et al., who observed weak or non-significant associations between maternal vitamin D and neonatal calcium despite strong maternal–neonatal vitamin D correlations[18,19].

Consistently, strong correlations in vitamin D status have been demonstrated by Panda et al. ($r = 0.622$), Boskabadi H et al. ($r = 0.672$), and Tsedendamba et al. ($r = 0.883$), with Jain et al. also showing significant association (p=0.013) [20–22] The underlying mechanism is explained by neonatal calcium physiology. During intrauterine life, calcium is actively transferred from the mother, and vitamin D crosses the placenta, making neonatal stores directly reflective of maternal status. After birth, this placental supply abruptly ceases, and calcium homeostasis depends on parathyroid hormone (PTH)–mediated mechanisms and vitamin D–dependent intestinal absorption. In vitamin D-deficient neonates, inadequate calcitriol production limits calcium absorption, predisposing to hypocalcemia. This mechanism becomes particularly relevant in LOH, where the infant relies entirely on enteral calcium absorption. Supporting this, Biswas R et al. reported elevated PTH levels in hypocalcemic infants with vitamin D deficiency, indicating a compensatory but insufficient response [23].

Additionally, Harrington et al. demonstrated that adequate vitamin D status attenuates the postnatal decline in calcium levels, further confirming its regulatory role [24]. This study has various limitations. The relatively small sample size and single-center design may limit generalizability. Lack of follow-up precludes assessment of long-term outcomes. Potential confounders such as maternal nutrition, feeding practices, and sunlight exposure were not fully evaluated. Additionally, the cross-sectional design does not allow causal inference between vitamin D deficiency and neonatal hypocalcemia.

Conclusion:-

In conclusion, neonatal hypocalcemia was relatively common and was more frequently observed among preterm infants, reinforcing prematurity as a key risk factor due to immature calcium regulatory mechanisms. A significant association was identified between hypocalcemia and vitamin D deficiency in both neonates and their mothers, underscoring the critical role of maternal vitamin D status in determining neonatal calcium homeostasis. The findings suggest that inadequate maternal vitamin D levels may contribute to reduced neonatal calcium reserves, particularly in the early postnatal period. These observations highlight the importance of ensuring adequate maternal vitamin D supplementation during pregnancy, along with early screening and timely management of at-risk neonates, especially in NICU settings. Such measures are essential to prevent complications and improve short- and long-term neonatal outcomes.

References:-

1. Oden J, Bourgeois M. Neonatal endocrinology. Indian J Pediatr. 2000;67(3):217–223.
2. Avşar H, Bülbül A, Baş EK, et al. Maternal–infant vitamin D coupling and neonatal hypocalcemia: a six-year cohort integrating preterm risk, onset timing, and pandemic effects. BMC Pediatr. 2026;26(1):134.
3. Aiims Protocols In Neonatology. 3rd ed. CBS Publishers and Distributors Pvt. Ltd.; 2023.
4. Cheng E, George AA, Bansal SK, et al. Neonatal Hypocalcemia: Common, Uncommon, and Rare Etiologies. NeoReviews. 2023;24(4):e217–e228.
5. Zhang H, Wang S, Tuo L, et al. Relationship between Maternal Vitamin D Levels and Adverse Outcomes. Nutrients. 2022;14(20):4230.
6. Kaushal M, Magon N. Vitamin D in pregnancy: A metabolic outlook. Indian Journal of Endocrinology and Metabolism. 2013;17(1):76–82.
7. Mansur JL, Oliveri B, Giacoia E, et al. Vitamin D: Before, during and after Pregnancy: Effect on Neonates and Children. Nutrients. 2022;14(9):1900.
8. Vuralli D. Clinical Approach to Hypocalcemia in Newborn Period and Infancy: Who Should Be Treated? International Journal of Pediatrics. 2019;2019:1–7.
9. Saha S, Mandal S, Halder A, et al. EPIDEMIOLOGY OF HYPOCALCAEMIA IN NICU OF A TEACHING HOSPITAL OF EASTERN REGION OF.
10. Shrestha NJ, Thapa M, Subedi KU, et al. Occurrence of Hypocalcaemia in Admitted Neonates in NICU. Med J Shree Birendra Hosp. 2021;20(2):156–161.
11. Elsary AY, Elgameel AA, Mohammed WS, et al. Neonatal hypocalcemia and its relation to vitamin D and calcium supplementation. Saudi Med J. 2018;39(3):247–253.
12. Alyasiri QKH. Prevalence of symptomatic hypocalcaemia in neonates in neonatal intensive care unit in Al-Diwaniyah city. 2021;25(12).
13. Seymen-Karabulut G, Günlemez A, Gökalp AS, et al. Vitamin D Deficiency Prevalence in Late Neonatal Hypocalcemia: A Multicenter Study. Jcrpe. 2021;13(4):384–390.
14. Nabiel N, Nugroho HW, Moelyo AG. Vitamin D Deficiency is Associated with Hypocalcemia in Preterm Infants. Mol Cell Biomed Sci. 2024;8(2):90.
15. Yılmaz B, Aygün C, Çetinoğlu E. Vitamin D levels in newborns and association with neonatal hypocalcemia. The Journal of Maternal-Fetal & Neonatal Medicine. 2018;31(14):1889–1893.
16. Sethi A, Priyadarshi M, Agarwal R. Mineral and bone physiology in the foetus, preterm and full-term neonates. Seminars in Fetal and Neonatal Medicine. 2020;25(1):101076.
17. Aasif Aziz Wani, Mohd Ashraf Bhat, Showkat Hussain Tali. Relationship between maternal Vitamin D levels and neonatal Vitamin D levels with delayed neonatal hypocalcemia - A hospital-based observational study. Asian J Med Sci. 2023;14(2):86–89.
18. Hashemipour S, Lalooha F, Zahir Mirdamadi S, et al. Effect of vitamin D administration in vitamin D-deficient pregnant women on maternal and neonatal serum calcium and vitamin D concentrations: a randomised clinical trial. Br J Nutr. 2013;110(9):1611–1616.

19. El Koumi MA, Ali YF, Abd El Rahman RN. Impact of maternal vitamin D status during pregnancy on neonatal vitamin D status. Turk J Pediatr. 2013;55(4):371–377.
20. Panda M, McIntosh J, Chaudhari T, et al. Do Maternal Vitamin D Levels Influence Vitamin D Levels in Preterm Neonates? Int J Pediatr. 2019;2019:8613414.
21. Boskabadi H, Heidari E. Correlation of Vitamin D Serum Level of Mothers and Their Newborns. Mod Care J [Internet]. 2021 [cited 2026 Apr 27];18(2).
22. Tsedendamba N, Zagd G, Radnaa O, et al. Correlation Between Maternal-Neonatal Vitamin D Status and it's Related to Supplementation in Mongolian Pregnant Women. ijirms. 2022;7(11):622–627.
23. Biswas R, Hasan AK. Hypocalcemic Seizures in Infancy and its Relationship with Maternal Vitamin D Deficiency. Dhaka Shishu (Child) Hosp J. 2022;37(2):98–102.
24. Harrington J, Perumal N, Al Mahmud A, et al. Vitamin D and fetal–neonatal calcium homeostasis: findings from a randomized controlled trial of high-dose antenatal vitamin D supplementation. Pediatr Res. 2014;76(3):302–309.