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**Correlation of Vitamin D and Calcium Concentration in Infant of Mother with High Risk of Vitamin D Deficiency****Irman Permana<sup>1\*</sup>, Faza Nurul Wardhani<sup>2</sup>, Raden Tina Dewi Judistiani<sup>3</sup>, Tetty Yuniati<sup>4</sup>, Budi Setiabudiawan<sup>5</sup>**Universitas Swadaya Gunungjati - Waled Regency Hospital, Cirebon, Indonesia<sup>1</sup>Department of Child Health Waled Regency Hospital, Cirebon, Indonesia<sup>2</sup>Universitas Padjadjaran, Sumedang, Indonesia<sup>3,4</sup>Universitas Padjadjaran, Hasan Sadikin General Hospital, Bandung, Indonesia<sup>5</sup>Email: irmanneo2018@gmail.com<sup>1</sup>.

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**KEYWORDS**

vitamin D, calcium, neonates, prevalence, concentration or levels, high risk

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**ABSTRACT**

Vitamin D deficiency is a significant concern during pregnancy, and its prevention is critical for neonatal health. However, there is a lack of comprehensive studies on screening vitamin D and calcium concentrations in neonates born to high-risk mothers. This study aimed to assess serum 25OHD and calcium concentrations in neonates from mothers previously identified as high risk for vitamin D deficiency, and to explore how these measurements might influence the management of such neonates. A cohort study, initiated in 2018 and continuing through 2023, was conducted using 241 venous blood samples from neonates aged 7 days. The concentrations of serum 25OHD and calcium were analyzed, and the relationship between the variables was evaluated using bivariate analysis and logistic regression. The results revealed a high prevalence of vitamin D insufficiency (85%, 30–50 nmol/L) and deficiency (37%, < 30 nmol/L) in neonates from this high-risk group. Additionally, a statistically significant and strong correlation ( $r: 0.965$ ,  $P < 0.05$ ) was observed between 25OHD and serum calcium concentrations. Interestingly, most venous samples collected within the first 24 hours postpartum exhibited hypercalcemia. These findings suggest that while vitamin D insufficiency and deficiency are common in neonates of high-risk mothers, the risk of neonatal hypocalcemia due to vitamin D deficiency is relatively low. Given the financial and physical burdens of neonatal blood screening, routine supplementation of vitamin D from birth, without the need for screening, may be a more efficient approach to managing this issue.

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DOI: 10.58860/ijsh.v3i9.237**Corresponding Author: Irman Permana\*****Email: irmanneo2018@gmail.com****INTRODUCTION**

Vitamin D deficiency, particularly in the form of 25 hydroxy-vitamin D (25OHD), is a widespread global health issue. Combined with insufficient calcium intake, it remains a leading cause of nutritional rickets and osteomalacia (Saggese et al. 2015). In severe cases, this condition leads to fractures and skeletal deformities in newborns and growing children, along with asymptomatic or symptomatic hypocalcemia that can result in cardiomyopathy, muscle spasms, and seizures (Högler 2015). While vitamin D plays a key role in maintaining calcium balance in the blood, growing evidence

suggests it may also influence various metabolic and physiological processes beyond bone health (Munns et al. 2016).

Certain populations, such as pregnant women with dark skin or those with limited UV exposure due to cultural attire, sunscreen use, or chronic disease, are particularly susceptible to vitamin D deficiency (Medeiros et al. 2016). The resurgence of nutritional rickets in countries like Australia, driven by immigration and increasing ethnic diversity, has placed a significant portion of the population at high risk for vitamin D and calcium deficiencies (Di Marco, Kaufman, and Rodda 2019). While either vitamin D or calcium alone may support bone mineralization, neonates, especially those born to vitamin D-deficient mothers, face a higher risk of hypocalcemia and associated complications (Pettifor and Thandrayen 2024). This study aimed to examine the relationship between vitamin D deficiency and calcium concentration in a cohort of preterm and term neonates, contributing to the growing understanding of neonatal health risks related to vitamin D.

## **METHOD**

A cohort study on the Role of Vitamin D in Efforts to Reduce Maternal and Infant Mortality Rates in Indonesia began in 2018 and will run until 2023. The study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Padjadjaran University. Details of the recruitment process are outlined in a previous report (Judistiani et al. 2018).

For this study, a sample of 241 preterm infants, aged 7 days, and their mothers was selected. Newborns with genetic malformations or syndromes were excluded from the sample. The inclusion criteria for mothers focused on those at high risk of vitamin D deficiency, identified through maternal serum 25OHD levels measured during the first trimester of pregnancy.

Anthropometric data and laboratory results were collected from the Maternal and Child Health Book (KIA). Maternal weight and height were used to calculate Body Mass Index (BMI, kg/m<sup>2</sup>), categorizing mothers into underweight (< 18.5 kg/m<sup>2</sup>), normal weight (18.5–24.9 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>), and obese (≥ 30 kg/m<sup>2</sup>). Newborns were classified as small for gestational age (SGA), appropriate for gestational age (AGA), or large for gestational age (LGA) using the Lubchenco curve, a standard clinical tool in Indonesia.

Both pregnant women and newborns had blood drawn from the medial cubital vein to measure levels of vitamin D, calcium, and magnesium (Tammo and Yıldız 2022). Vitamin D levels were categorized as deficient (<20 ng/mL), insufficient (20–29.99 ng/mL), or normal (≥30 ng/mL), following guidelines from Munns et al. (2016). Bivariate analysis and logistic regression were performed to explore the relationships between these variables.

### **Statistical analyses**

Data were compiled into Excel® spreadsheets, which included identification information, general characteristics, anthropometric data, and laboratory results. The data were then revised, consolidated, and transferred into the Statistical Package for Social Sciences, version 25.0 (IBM®) for analysis. Categorical variables were described using frequencies and percentages, while continuous variables were presented using medians, means, standard deviations, or ranges (Rucker, McShane, and Preacher 2015).

The relationship between 25OHD and calcium was examined using chi-square, t-test, Pearson's correlation, and Spearman's correlation. The t-test was employed for gender differences (male vs. female), while chi-square and cross-tabulation were used for categorical variables such as birth weight, gestational age, and calcium levels. Correlation coefficients and scatter plots were used for continuous variables. A p-value of less than 0.05 was considered statistically significant.

**RESULT AND DISCUSSION**

This study involved 241 respondents consisting of neonates. The analysis results show that most of the respondents were male (52.8%). Most respondents are term neonates (62.2%). The majority of the respondents who participated had normal birth weights (59.8%).

**Table 1.**  
**Variable**

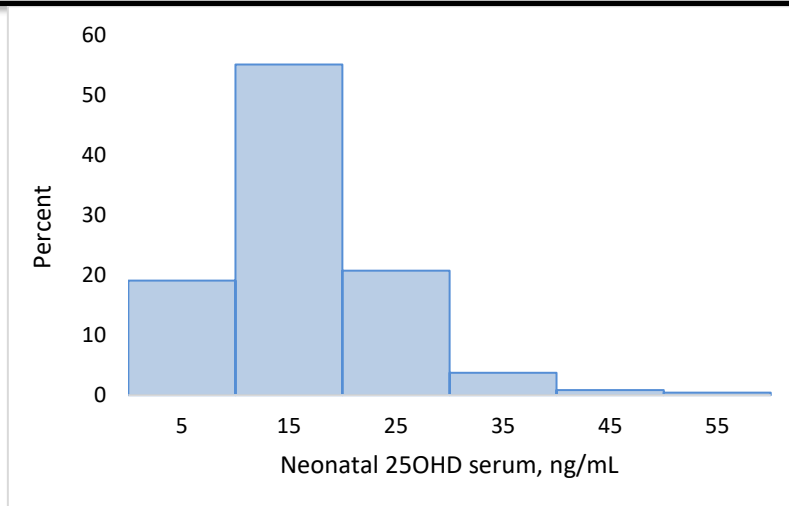
Variable		Frequency	Percent
Gender	Female	114	47.2
	Male	127	52.8
Term	Pre-term (<37 weeks)	91	37.8
	Term (≥37 weeks)	150	62.2
Birth weight	Low (<2500)	97	40.2
	Normal (≥ 2500)	144	59.8

Table 2 shows that the gender distribution was nearly equal in the sample of 241. Neonates were predominantly born at term gestation (≥ 37 weeks) with a mean age of 38.7 weeks and were predominantly of normal birth weight (≥ 2500 g) with a mean birth weight of 2593.6 g

**Table 2.**  
**Statistical Analysis of Variable**

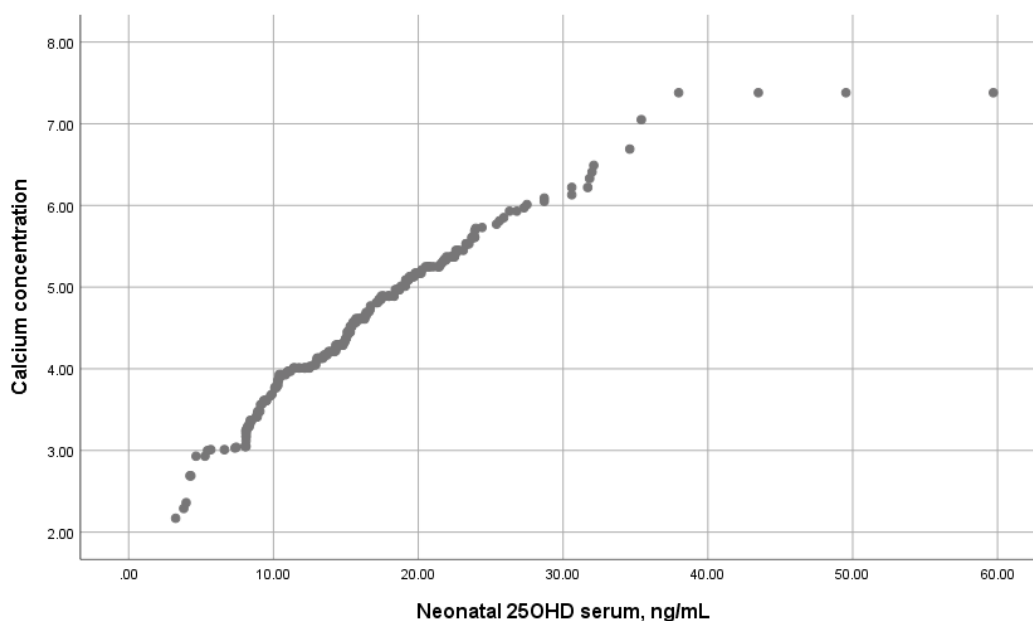
Variable	Number (n)	Mean	SD	Median	Lower quartile	Upper quartile	Min	Max
Gestational age (weeks)	241	36.6	3.5	38	34	39	28	42
Birth Weight (grams)	241	2593.6	758	2800	1980	3200	785	4130
25OHD (nmol/l)	241	16.6	7.5	15.3	11	20.2	3.24	59.71
Calcium (mmol/l)	241	4.55	0.96	4.52	3.97	5.17	2.17	7.38

According to the classification of vitamin D deficiency from the International Global consensus guidelines 2016, vitamin D levels were sufficient (25OHD > 50 nmol/L) in 39% of neonates, insufficient (25OHD 30–50 nmol/L) in 85% and deficient (25OHD < 30 nmol/L) in 37%. Figure 1 indicated a high prevalence of vitamin D insufficiency and deficiency in preterm and term infant.



**Figure 1. Distribution of serum 25 hydroxy-vitamin D (nmol/L)**

Figure 2 indicated that there was a strong significant correlation between vitamin D and corrected calcium concentrations ( $r = 0.965$ ,  $P < 0.05$ ) (Fig. 3). Nearly all the hypercalcaemic values were those of venous samples collected on the first day of life. The standard reference range used in the laboratory at Padjajaran University is 2.25–2.65 mmol/L.



**Figure 2. Scatter plot showing the relationship between serum 25 hydroxy-vitamin D (nmol/L) and calcium concentration (mmol/L) with Pearson correlation ( $r = 0.965$ ,  $p < 0.05$ )**

Our study is the first in Indonesia, to our knowledge, to examine the practice of screening neonates from high-risk mothers for vitamin D deficiency and calcium concentration. A strong positive correlation between calcium concentration and vitamin D serum in infants is found in this study. Meanwhile, the absence of birth variables and neonatal 25OHD concentrations from our data is found in other studies (Richard, Rohrmann, and Quack Lötcher 2017). Our findings, nevertheless, revealed a greater rate of vitamin D insufficiency and deficiency than what Young et al. had previously documented in Australia (Young et al. 2012) and is comparable to prevalence recorded in mixed ethnic

populations of other Western nations (Munns et al. 2016). The high prevalence of vitamin D deficiency is documented in regions at high latitudes with a majority of fair-skinned people and in other studies of mainly white ethnic populations (Dalgård et al. 2016). As a result, it would appear that there is no need to measure 25OHD in newborns at high risk since vitamin D deficiency is more common in these populations (Bennett and Kearney 2018).

In this study, only a quarter of the neonates were vitamin D sufficient on testing. Nonetheless, exclusively breastfed or sufficiently fed formula-fed infants are at greater risk of developing vitamin D deficiency (Lykkedegn et al. 2017). Hence, most international guidelines recommend oral supplementation with vitamin D for all infants (Marshall et al. 2016). The major challenge to daily infant cholecalciferol supplementation remains poor adherence (Vinkhuyzen et al. 2016), which is substantially improved with education and emphasis on cholecalciferol supplementation from health care providers or paediatricians in the early post-partum period (Randev, Kumar, and Guglani 2018). We found an overall non-significant correlation between 25OHD and corrected calcium. This is conversely different from the study where they documented serial measurements of total calcium and 25OHD levels in term and premature neonates (Yılmaz, Aygün, and Çetinoğlu 2018). The correlation between neonatal vitamin D levels and neonatal hypocalcemia at birth, nevertheless, is not clear in the literature (Kozgar, Chay, and Munns 2020). Vitamin D deficiency is highly prevalent in our mixed ethnicity population, and neonatal screening of vitamin D levels affirms what is largely known. A different approach to supplementing these babies with cholecalciferol in the absence of routine testing appears to provide superior value.

The current study's findings are not conclusive, but further research is needed to identify preterm newborn vitamin D status (Tous et al. 2020). Notably, the piecewise linear regression model enables the adjustment of confounding variables, which might be numerous in preterm baby clinical studies. The study was limited because we did not have complete maternal data for a couple of mother-infant groups and did not compare maternal vitamin D status during pregnancy to neonatal 25OHD and calcium levels. Since calcium, phosphorus, and vitamin D are interrelated, improvements in vitamin D delivery are associated with improvements in calcium and phosphorus delivery. This complementary increase in delivery complicates the identification of causality. This comprehensive assessment of preterm and term infants serves as a framework for further study, including vitamin D supplementation approaches to maintain calcium and phosphorus balance and good bone mineralization (Gharibeh 2021). Validation studies are needed. Thus, greater investigation into the complicated role of vitamin D in calcium, phosphorus, and bone in the growing, developing neonates.

## **CONCLUSION**

Our study confirms a significant prevalence of vitamin D deficiency in our mixed-ethnic population, as evidenced by newborn screening. While blood testing for vitamin D levels in newborns requires an invasive procedure that causes discomfort for both babies and parents, and adds to hospital resource demands, our findings indicate a low incidence of hypocalcemia in these healthy newborns with vitamin D deficiency at birth. Importantly, our results suggest that vitamin D supplementation is an effective and easily implementable intervention to address this deficiency. Based on these findings, we recommend routine vitamin D supplementation for newborns, especially in populations at risk of deficiency, as a preventive measure to improve neonatal health outcomes and reduce the need for invasive screening.

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