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Serum Vitamin D Levels in Neonates and Their Mothers at Birth: A Comparative Analysis Highlighting Need for Therapeutic Strategies

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Abstract

Objective: Objective: The study was conducted to examine serum vitamin D levels in preterm and full-term neonates and their mothers at birth to explore potential associations.

Methods: A cross-sectional analytical study was carried out in the Pediatrics and Obstetrics departments of Khyber Teaching Hospital, Peshawar from May 2022 to Nov 2022. After taking institutional approvals, 198 healthy pre-term and full-term neonates and their mothers were enrolled in the study. A structured proforma comprising demographic data was filled and samples of blood were obtained from the mothers at birth and the neonates within 72 hours of birth. Serum levels of Vitamin D were determined by ELISA and based on these levels the subjects were classified as sufficient, insufficient, or deficient.

Results: Of 198 infants studied, 77.8% were full-term and 22.2% were preterm. Males comprised 57.1% of the sample. A majority, 74.2% came from poor socioeconomic backgrounds, with 62.6% of mothers being uneducated. Both preterm and full-term infants predominantly exhibited vitamin D deficiency. Among 44 mothers of preterm and 154 mothers of full-term infants, vitamin D levels differed significantly (p=0.003). However, in both groups, there was a higher prevalence of mothers with insufficient vitamin D levels compared to those with adequate levels. Significant associations (p=0.001 and 0.003) suggest maternal vitamin D levels may influence neonatal vitamin D status and risk of preterm labour.

Conclusion: A notable proportion of mothers exhibited deficient levels of vitamin D, and correspondingly, their neonates also displayed deficient levels. A potential correlation between maternal Vitamin D status and the occurrence of preterm labour was also observed.

Keywords: Mother, Neonate, Pediatrics, Vitamin D.

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1. Introduction

Vitamin D is a fat-soluble vitamin which plays a vital role in preserving the body's health and functionality. Its deficiency is recognized as a prevalent health concern in our population, with significant implications for overall health and well-being.[1] Although we have plentiful sunshine, deficiency of vitamin D is widespread in all age groups, among all genders and geographic locations. Its prevalence in the Pakistani adult population is approximately 53.5% while the overall prevalence is about 31.2%.[2] Another study conducted on neonates and infants in northern India reported this prevalence to be around 75%.[3]

Vitamin D supplementation is required in all age groups, especially in reproductive age. It has long-term effects on the neonatal immune system and its deficiency may affect both innate and adaptive immune systems.[4] Vitamin D is important for the development of fetal bones during pregnancy, as well as for supporting overall growth and development throughout gestation.[5, 6] Compromised Vitamin D status in mothers is associated with around two-fold increase in congenital heart defects in offspring.[7, 8] A normal maternal level also helps in the prevention of neonatal sepsis.[9] Other manifestations of vitamin D deficiency may include hypo-calcemic seizures and tetany in early infancy. Its deficiency may elevate the risk of Type 1 diabetes mellitus and other endocrine disorders in children.[10] Studies have found that vitamin D deficiency independently increases the risk of respiratory distress syndrome (RDS) in premature infants.[11] Some researchers also associate its deficiency with inflammatory skin conditions especially atopic dermatitis in neonates and children.[12]

Prematurity, a significant factor contributing to infections, impaired bone development, and growth disturbances, has not been thoroughly investigated for its correlation with vitamin D levels on a larger scale. Moreover, given the critical role of maternal Vitamin

D levels in fetal development, neonatal Vitamin D levels are typically not evaluated at birth in our community. So, it is important to examine the association between maternal and neonatal vitamin D levels. A study was required to fill a crucial gap in understanding the relationship between prematurity, maternal Vitamin D levels, and neonatal Vitamin D status, contributing to enhanced maternal and neonatal care practices. This study aimed to assess the serum Vitamin D levels in preterm and full-term neonates and their mothers at birth for any possible associations.

2. Materials & Methods

A cross-sectional analytical study was carried out in the Pediatrics and Obstetrics departments of Khyber Teaching Hospital, Peshawar from May 2022 to Nov 2022. A sample size of 198 was calculated by the WHO formula with a prevalence of disease taken as 75%.[3] Sampling was carried out using a non-probability convenient technique. After obtaining approval of the project from concerned institutes vide letter number 9249/PGMED/KGMC and DIR/KMU-AS&RB/CS/001660 and NOC from the administration of the hospital (312/DME/KMC), healthy pre-term and full-term neonates (born before and after 37 weeks of gestation, respectively) and their mothers were enrolled in the study. Neonates with clinical signs of sepsis or on treatment for apnea, bradycardia, convulsions, lethargy, respiratory distress, poor reflexes, abdominal distension, and inability to feed, and mothers with chronic illness or on hormonal replacement therapy were excluded.

After obtaining informed consent from the parents, a structured proforma comprising demographic data was filled and samples of blood were obtained from the mothers at birth and the neonates within 72 hours of birth under sterile conditions. The samples were centrifuged (AI-IE CHINA) at a speed of 3000 revolutions/minute for 10 minutes. Serum levels of Vitamin D were measured by enzyme-linked immunosorbent assay using an ELISA kit (Abbot-Architect-USA) and Roche Diagnostic COBAS C311 analyzer (Hitachi Manheim, Germany) according to the manufacturer's instruction manual. Based on these levels, the subjects were classified as sufficient (levels above 30 ng/ml), insufficient (levels between 20-30 ng/ml, and deficient (levels below 20 ng/ml).[13, 14]

Data was analyzed in the SPPS version 25. Descriptive categorical variables like the birth status of the infant, gender, socioeconomic status, type of living, and education of the mother were calculated as frequency and percentages. Descriptive numerical variables like the weight of neonates and Vitamin-D level of pre-term and full-term neonates and their mothers were calculated as mean and SD (standard deviation). The Chi-square test was employed to compare the Vitamin D levels of neonates and their mothers. A threshold of $P \leq 0.05$ was deemed statistically significant.

3. Results

An analysis of 198 subjects indicated that the majority of infants, 154 (77.8%) were born full-term, whereas 44 (22.2%) were preterm. Regarding the distribution of gender and birth weight, most of the neonates had a birth weight of 3 kg (59.1%), followed by 4 kg (24.2%). Additionally, male neonates accounted for a larger proportion of 57.1% compared to female neonates (42.9%). The socioeconomic data indicated that a significant portion of 74.2% come from poor socioeconomic backgrounds. A greater percentage of mothers were uneducated (62.6%) than those who were educated (37.4%). The data also provided insight into the living conditions of the mothers in the study population. Most of the cases (66.2%) were residents of rural areas with a majority living in open houses (61.6%).

Table 1: Distribution of Vitamin D levels in neonates

Vitamin D levels (Neonatal)	Pre-Term n (%)	Full Term n (%)	Total	P value
Sufficient	10 (22.7)	35 (22.7)	45 (22.7)	0.19
Insufficient	9 (20.4)	16 (10.3)	25 (12.6)	
Deficient	25 (56.8)	103 (66.8)	128 (64.6)	
Total	44 (100)	154 (100)	198 (100)	

Table 1 illustrates the distribution of vitamin D levels among pre-term and full-term infants, revealing a predominant deficiency in vitamin D levels across both categories. Full-term infants showed a higher proportion of sufficient vitamin D levels compared to preterm infants. However, these differences in proportions across groups were statistically not significant with a p-value of 0.19.

There were 44 mothers of pre-term infants and 154 mothers of full-term infants. Upon stratification, statistically significant differences were observed among sufficient, insufficient, and deficient Vitamin D

level groups (Table 2). Both pre-term and full-term groups revealed a higher frequency of mothers with lower Vitamin D levels (insufficient and deficient) compared to those with sufficient levels.

Table 2: Distribution of maternal Vitamin D levels in pre-term and full-term neonates

Vitamin D levels (Maternal)	Pre-Term n (%)	Full Term n (%)	Total n (%)	P value
Sufficient	10 (22.7)	28 (18.1)	38 (19.1)	0.003
Insufficient	14 (31.8)	19 (12.3)	33 (16.6)	
Deficient	20 (45.4)	109 (70.7)	129 (65.1)	
Total	44 (100)	154 (100)	198 (100)	

Table 3 presents the statistical analysis, suggesting a noteworthy association between maternal and neonatal vitamin D levels, supported by a p-value of 0.001. There were 31 cases where both had a sufficient level, 14 cases with insufficient levels and 118 cases with deficient levels of Vitamin D. This implies a strong correlation, indicating that the vitamin D levels in mothers are closely linked to those in their infants.

Table 3: Association between maternal and neonatal Vitamin D levels

Vitamin D levels (Neonatal)	Vitamin D Levels (Maternal)			Total	P value
	Sufficient	Insufficient	Deficient		
Sufficient	31	9	5	45	0.001
Insufficient	5	14	6	25	
Deficient	0	10	118	128	
Total	36	33	129	198	

The data from Table 4 suggests a notable association between maternal vitamin D levels and the occurrence of preterm labour. Specifically, out of 44 pre-term births, 20 were observed in mothers with deficient levels of vitamin D. These findings underscore the potential impact of maternal vitamin D status on the occurrence of pre-term labour.

Table 4: Association between maternal Vitamin D level and pre-term birth

Vitamin D levels (Maternal)	Pre-Term Birth			P value
	Yes	No	Total	
Sufficient	10	26	36	0.003
Insufficient	14	19	33	
Deficient	20	109	129	
Total	44	154	198	

4. Discussion

The prevalence of Vitamin D deficiency is a significant global health issue, especially affecting pregnant women in South Asian and Middle Eastern demographics.[15, 16] Rather It has been identified as an epidemic among South Asian populations and in Western countries.[17] The objective of this study was a comparison of Vitamin D levels of neonates with pregnant women at pre-term and full-term births. The study revealed that the majority of mothers (65.1%) had a deficiency in vitamin D. This high prevalence of deficiency is concerning with findings aligning closely with those of another study conducted in Karachi.[16] Current study demonstrated Vitamin D sufficiency in 19.1% of mothers and 22.7% of neonates whereas Vitamin D deficiency in 65.1% of mothers and 64.6 % of neonates. In one of the studies, more than half of Vitamin D deficient cases were found in neonates born to deficient mothers.[18] These findings highlight maternal Vitamin D deficiency as a crucial factor contributing to the deficiency of Vitamin D in neonates. Our results are in agreement with findings of other studies conducted in Turkey reporting Vitamin D deficiency in 54% of the mothers and 80% of the neonates[19] and in Saudi Arabia, where 59% of mothers and 70% of newborns were severely deficient.[20] Another cross-sectional study reported a deficiency of vitamin D in 88% of infants, which aligns with our findings when combining cases of deficiency and insufficiency.[21]

Numerous studies have focused on investigating how maternal Vitamin D levels influence adverse pregnancy outcomes. However, findings differ based on the participants studied and the relationship between Vitamin D status and pre-term births.[22-24] In this study there was a significant correlation between maternal Vitamin D levels and pre-term labor with a p-value of 0.003. This underscores the potential influence of maternal Vitamin D status on the occurrence of preterm labour. A meta-analysis exclusively comprising longitudinal studies confirmed that mothers with Vitamin D concentrations below 30 ng/mL faced an 83% higher risk of delivering prematurely.[25] Additionally, research has demonstrated the benefits of Vitamin D supplementation in reducing the likelihood of preterm birth.[26] For instance, Wagner et al. reported a 60% decrease in premature births in the U.S. when Vitamin D concentrations exceeded 40 ng/mL in 2016, advocating

for a recommended supplementation of at least 4000 IU/day to achieve these levels.[23] Conversely, a cohort study in China found no significant correlation between lower Vitamin D levels in pregnant women and premature births, suggesting that measuring vitamin D levels alone may not suffice to predict preterm births.[27]

Vitamin D deficiency is speculated to be due to different reasons including genetics of South Asians, but it has yet to be explored.[28] The current study revealed majority of participants have poor socioeconomic status. The non-affordability of Vitamin D supplements could promote lower levels of this nutrient. In Pakistan, fish oil, the major dietary source of Vitamin D, is perceived as expensive and not commonly consumed. Moreover, unlike in many countries where milk and milk products are fortified with Vitamin D, milk in Pakistan is largely unprocessed and lacks added nutrients. Hence, dietary habits in Pakistan often do not ensure adequate vitamin D intake. The current study revealed that a higher percentage of mothers were uneducated, which could contribute to adverse impacts on their health and their neonates' health. Because of better awareness about balanced diet, Vitamin D supplements, sunshine exposure, and access to healthcare services, a study reported Vitamin D status better in educated than uneducated mothers.[27] The results of the current study suggest that pregnant women of our study population should be considered as candidates for Vitamin D prophylaxis. Supplementing with 4000 IU/day of Vitamin D was found to be more effective in increasing serum levels of Vitamin D in both mothers and their infants compared to a dosage of 2000 IU/day.[29]

We acknowledge that the potential for bias and unmeasured confounders exists in this study which may limit the generalizability of findings. Furthermore, the exclusion of preterm neonates with complications reduced the number of preterm cases, impacting our ability to draw robust conclusions about the relationship between maternal vitamin D deficiency and preterm labour. However, a well-designed study with a prospective longitudinal approach incorporating calcium and Vitamin D dietary status throughout gestation will provide a holistic overview of changes and their impact on neonates.

5. Conclusion

The findings of this study highlight the substantial influence of maternal Vitamin D levels on neonates. A considerable proportion of mothers in our study population exhibited vitamin D deficiency, and their neonates similarly showed deficient levels. Furthermore, our findings suggest a potential link between maternal vitamin D status and the incidence of preterm labour, with a notable number of preterm births associated with maternal deficiency. These results underscore the critical importance of addressing maternal vitamin D deficiency in prenatal care to enhance neonatal health outcomes.

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