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Maternal Vitamin-D Status in Early Pregnancy and Infant Neurodevelopmental Outcomes: A Prospective Cohort Study Using the Bayley-Iii Scale

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ABSTRACT

Background: Vitamin D plays a vital role in foetal brain development and neurocognitive maturation. Maternal vitamin D deficiency during pregnancy has been associated with adverse developmental outcomes in offspring; however, evidence from Indian populations remains limited. This study aimed to evaluate the association between maternal vitamin D status during early pregnancy and infant neurodevelopmental outcomes at 12 months of age.

Materials and methods: This prospective cohort study consists a total of 344 pregnant women recruited during the first trimester (≤14 weeks gestation). Maternal serum 25-hydroxyvitamin D [25(OH)D] levels were measured and categorized as deficient (<20 ng/mL), insufficient (20-29 ng/mL), or sufficient (≥30 ng/mL). Infants were followed until 12 months of age and assessed using the Bayley Scales of Infant and Toddler Development, Third edition (Bayley-III). Cognitive, language, and motor composite scores were compared across maternal vitamin D categories.

Results: The mean maternal serum vitamin D concentration was 21.6±8.4 ng/mL. Vitamin D deficiency was present in 44.8% of participants, insufficiency in 32.6%, and sufficiency in 22.7%. Infants born to vitamin D sufficient mothers demonstrated significantly higher cognitive (105.4±9.6), language (102.9±9.7), and motor (105.8 ± 8.9) scores compared with those born to deficient mothers (93.9±10.8, 90.8±11.5, and 95.0±10.1, respectively; $p<0.001$). Maternal vitamin D levels correlated positively with cognitive ($r=0.42$), language ($r=0.39$), and motor scores ($r=0.36$) ($p<0.001$). Multiple regression analysis identified maternal vitamin D concentration as an independent predictor of cognitive development ($\beta=0.38$, $p<0.001$).

Conclusion: Maternal vitamin D status during early pregnancy is significantly associated with infant neurodevelopmental outcomes. Adequate vitamin D levels were linked to improved cognitive, language, and motor development, highlighting the importance of early screening and appropriate supplementation during pregnancy.

Keywords: *Vitamin D, Maternal Nutrition, Neurodevelopment, Bayley-III, Cognitive Development, Infant Development.*

INTRODUCTION

Vitamin D is a fat-soluble secosteroid hormone traditionally recognized for its role in calcium homeostasis and skeletal development. However, growing evidence suggests that vitamin D exerts important effects on the developing central nervous system, influencing neuronal differentiation, synaptogenesis, neurotrophic signalling, and neurotransmitter synthesis during foetal life [1,2]. The presence of vitamin D receptors and vitamin D-metabolizing enzymes in various regions of the foetal brain supports its critical role in neurodevelopmental processes [3].

Vitamin D deficiency is a widespread public health concern among pregnant women worldwide, particularly in developing countries where nutritional inadequacies, limited sunlight exposure, and sociocultural practices contribute to suboptimal vitamin D status [4]. Studies from India have reported a high prevalence of maternal vitamin D deficiency, with estimates ranging from 50% to 90% among pregnant women [5]. Maternal vitamin D deficiency during pregnancy has been associated with adverse maternal and neonatal outcomes, including preeclampsia, gestational diabetes, preterm birth, low birth weight, and impaired skeletal growth in offspring [6,7].

In recent years, increasing attention has been directed toward the potential association between prenatal vitamin D exposure and infant neurodevelopment. Experimental studies suggest that inadequate vitamin D levels during critical periods of brain development may alter neuronal maturation and cognitive functioning [8]. Observational cohort studies have demonstrated associations between low maternal vitamin D concentrations and poorer cognitive, language, behavioral, and motor outcomes in children, although findings remain inconsistent across populations and age groups [9,10]. Variations in study design, timing of vitamin D assessment, developmental evaluation tools, and adjustment for confounding factors may account for these discrepancies.

The Bayley Scales of Infant and Toddler Development (Bayley-III) are among the most widely accepted instruments for evaluating early childhood neurodevelopment, providing standardized assessments of cognitive, language, and motor performance [11]. Early identification of developmental vulnerabilities is crucial for implementing timely interventions that may improve long-term outcomes.

Despite the high burden of vitamin D deficiency in India, prospective evidence examining its influence on infant neurodevelopment remains limited. Therefore, the present study was undertaken to evaluate maternal vitamin D status during early pregnancy and its association with neurodevelopmental outcomes in infants at 12 months of age using the Bayley-III assessment scale. The findings may contribute to a better understanding of the role of maternal nutrition in optimizing early childhood development.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Department of Paediatrics in collaboration with the Department of Obstetrics and Gynaecology at MNR Medical College and Hospital, Sangareddy, Telangana, India from April 2024 to March 2026 following approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrolment. Pregnant women attending the antenatal outpatient clinic during the first trimester of pregnancy (≤14 weeks of gestation) were screened for eligibility. Women with singleton pregnancies who intended to deliver and continue follow-up at the study institution were recruited consecutively. A total of 344 pregnant women were enrolled and followed until delivery. Their infants were subsequently monitored for neurodevelopmental assessment during infancy.

Inclusion Criteria: Pregnant women aged between 18-40 years, singleton pregnancy confirmed by ultrasonography, gestational age ≤14 weeks at recruitment, willing to participate and provide informed consent and availability for follow-up until infant neurodevelopmental evaluation.

Exclusion Criteria: Multiple pregnancies, known foetal congenital anomalies, pre-existing maternal neurological or psychiatric disorders, chronic renal disease, severe liver disease, malabsorption syndromes, maternal use of medications known to affect vitamin D metabolism and infants with major congenital malformations or severe neonatal complications affecting neurodevelopmental assessment.

Baseline maternal demographic and clinical information were recorded using a structured questionnaire. Obstetric history and relevant medical information were obtained from hospital records. A 5ml of peripheral venous blood was collected from participants during early pregnancy (≤14 weeks gestation). Serum was separated and stored at -20°C until analysis. Maternal vitamin D status was determined by measuring serum 25-hydroxyvitamin D [25(OH)D] concentrations using a chemiluminescent immunoassay. Participants were categorized according to serum 25(OH)D levels as deficient (<20 ng/mL), insufficient (20-29 ng/mL) and sufficient (≥30 ng/mL).

Infants born to enrolled mothers were followed prospectively from birth. Birth-related variables including gestational age, birth weight, sex, mode of delivery, and neonatal complications were recorded. Neurodevelopmental outcomes were evaluated at 12 months of corrected age using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III). Assessments were performed by trained pediatric developmental specialists who were blinded to maternal vitamin D status.

The Bayley-III evaluates the following developmental domains including cognitive development, language development (receptive and expressive communication) and motor development (fine and gross motor skills). Composite scores for

each domain were calculated according to standardized guidelines. Higher scores indicated better developmental performance.

Statistical Analysis

The collected data was extracted into Microsoft Excel sheet and analyzed using SPSS v.26.0. Continuous variables were expressed as mean and standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons among vitamin D status groups were performed using one-way ANOVA for continuous variables and Chi-square test for categorical variables. Independent sample t-test was used for two-group comparisons where appropriate. Pearson's correlation analysis was employed to evaluate the relationship between maternal serum 25(OH)D concentrations and Bayley-III composite scores. Multiple linear regression analysis was performed to determine the independent effect of maternal vitamin D status on infant neurodevelopment. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Maternal baseline characteristics (n=344)

Maternal baseline variable	Category	Number (%) / Mean ± SD
Maternal age (years)	Mean±SD	26.8±4.3
	18-24 years	126 (36.6%)
	25-29 years	142 (41.3%)
	30-34 years	58 (16.9%)
	≥35 years	18 (5.2%)
Body mass index (kg/m²)	Mean±SD	24.7±3.9
Parity	Primigravida	158 (45.9%)
	Multigravida	186 (54.1%)
Educational status	Illiterate	22 (6.4%)
	Primary school	54 (15.7%)
	Secondary school	136 (39.5%)
	Graduate	102 (29.7%)
	Postgraduate	30 (8.7%)
Occupation	Homemaker	218 (63.4%)
	Agricultural worker	44 (12.8%)
	Skilled worker	32 (9.3%)
	Private sector	28 (8.1%)
	Government sector	22 (6.4%)
Socioeconomic status (Modified Kuppuswamy Scale)	Upper	24 (7%)
	Upper middle	78 (22.7%)
	Middle	128 (37.2%)
	Lower middle	84 (24.4%)
	Lower	30 (8.7%)
Residence	Rural	208 (60.5%)
	Urban	136 (39.5%)
Average daily sunlight exposure	<15 minutes/day	92 (26.7%)
	15-30 minutes/day	106 (30.8%)
	>30 minutes/day	146 (42.4%)
Physical activity	Sedentary	154 (44.8%)
	Moderate	142 (41.3%)
	Active	48 (14%)
Vitamin D supplementation during pregnancy	Yes	168 (48.8%)
	No	176 (51.2%)
Calcium supplementation	Yes	224 (65.1%)
	No	120 (34.9%)
Gestational age at recruitment (weeks)	Mean±SD	11.2±1.8
Haemoglobin level (g/dl)	Mean±SD	10.9±1.3
History of gestational diabetes mellitus	Present	32 (9.3%)
History of pregnancy-induced hypertension	Present	26 (7.6%)
Serum 25(OH)D concentration (ng/mL)	Mean±SD	21.6±8.4

Table 2: Distribution of maternal vitamin-D status.

Vitamin D Category	Serum 25(OH)D (ng/mL)	Frequency (%)
Deficient	<20	154 (44.8%)
Insufficient	20–29	112 (32.6%)
Sufficient	≥30	78 (22.7%)

Table 3: **Neonatal Characteristics.**

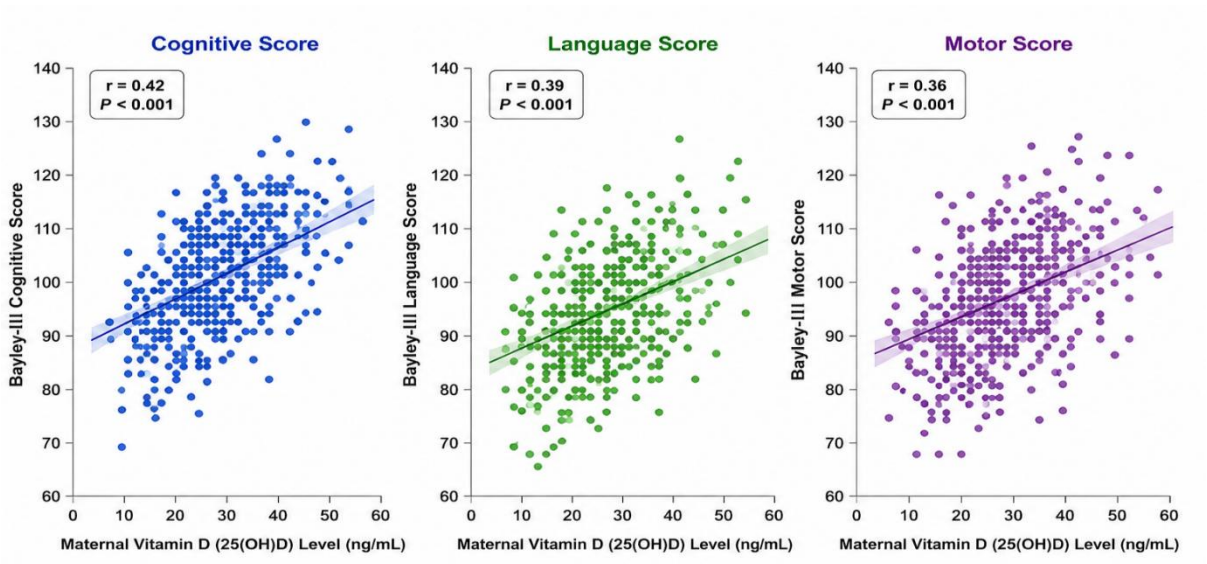
Variable	Mean ± SD / n (%)
Gestational age at birth (weeks)	38.5±1.3
Birth weight (kg)	2.92±0.41
Male infants	178 (51.7%)
Female infants	166 (48.3%)
Vaginal delivery	218 (63.4%)
Caesarean section	126 (36.6%)
NICU admission	28 (8.1%)

Table 4: Bayley-III composite scores at 12 Months

Domain	Bayley-III score
	Mean ± SD
Cognitive Score	97.8±11.6
Language Score	95.1±12.3
Motor Score	98.6±10.8

Table 5: Bayley-III Scores according to maternal Vitamin D status.

Domain	Deficient (n=154)	Insufficient (n=112)	Sufficient (n=78)	P-value
Cognitive score	93.9 ± 10.8	98.7 ± 10.2	105.4 ± 9.6	0.001
Language score	90.8 ± 11.5	95.6 ± 10.8	102.9 ± 9.7	0.001
Motor score	95.0 ± 10.1	99.2 ± 9.8	105.8 ± 8.9	0.001



Graph 1: Correlation between maternal Vitamin D levels and Bayley-III scores.

Maternal serum vitamin D concentration showed moderate positive correlations with all developmental domains (Graph 1). The regression model explained 31.8% of the variance (Adjusted $R^2 = 0.318$) in cognitive development scores. Maternal vitamin D concentration remained an independent predictor after adjustment for potential confounders (Table 6).

Table 6: Multiple linear regression analysis for predictors of cognitive development.

Variable	β Coefficient	95% CI	p-value
Maternal Vitamin D level	0.38	0.24-0.52	0.001
Maternal education	0.21	0.08-0.34	0.002
Birth weight	0.18	0.05-0.29	0.006
Maternal age	0.07	-0.04-0.16	0.148

BMI	-0.05	-0.13-0.08	0.302
Gestational age at delivery	0.09	-0.03-0.19	0.087

Table 7: Risk of developmental delay according to maternal vitamin D status

Vit-D Status	Developmental delay	OR (95% CI)	p-value
Sufficient	4 (5.1%)	-	-
Insufficient	12 (10.7%)	2.23 (0.69-7.18)	0.173
Deficient	34 (22.1%)	5.26 (1.82-15.18)	0.002

DISCUSSION

In present study, 44.8% of pregnant women were vitamin D deficient, while only 22.7% had sufficient vitamin D levels. This observation is consistent with previous reports indicating widespread vitamin D deficiency among pregnant women, particularly in South Asian populations. Sachan et al. reported a prevalence exceeding 60% among pregnant women in northern India, while other Indian studies have documented deficiency rates ranging from 50% to 90% depending on geographical location, dietary habits, and sunlight exposure [5,12]. The high prevalence observed in our cohort underscores the continued public health importance of maternal vitamin D insufficiency despite increasing awareness and supplementation programs.

In present study the significant difference in Bayley-III cognitive, language, and motor scores across maternal vitamin D categories. Infants born to mothers with sufficient vitamin D levels exhibited superior developmental performance compared with those born to deficient mothers. These findings support the biological plausibility that vitamin D contributes to foetal brain development through regulation of neurotrophic factors, neuronal differentiation, axonal connectivity, and neurotransmitter synthesis [2, 3]. Experimental studies have shown that vitamin D receptors are widely distributed throughout the developing brain, including regions involved in cognition and motor control, providing mechanistic support for the observed associations [8].

The positive correlations identified between maternal vitamin D concentrations and Bayley-III scores further strengthen the evidence for a dose-response relationship. Cognitive development demonstrated the strongest correlation (r=0.42), followed by language (r=0.39) and motor development (r=0.36). Similar findings were reported by Morales et al., who observed that higher maternal vitamin D levels during pregnancy were associated with improved mental and psychomotor development in early childhood [10]. Likewise, Whitehouse et al. found that maternal vitamin D deficiency was linked to poorer neurocognitive performance and language outcomes in offspring [9]. These observations collectively suggest that adequate prenatal vitamin D availability may contribute to optimal neurological maturation.

In present study multivariable regression analysis revealed that maternal vitamin D concentration, maternal education, and birth weight were independent predictors of cognitive development. Among these variables, maternal vitamin D exhibited the strongest standardized coefficient. This finding is in agreement with cohort studies demonstrating that prenatal nutritional status can influence developmental trajectories independent of socioeconomic and perinatal factors [13]. Maternal education also emerged as a significant determinant, reflecting the established influence of environmental stimulation, caregiving practices, and health literacy on early childhood development [14]. Similarly, higher birth weight was associated with improved cognitive outcomes, consistent with previous evidence linking fetal growth with subsequent neurodevelopmental performance [15].

The adjusted regression model explained approximately 31.8% of the variance in cognitive scores, indicating that neurodevelopment is influenced by multiple biological, environmental, genetic, and socioeconomic factors. Nevertheless, the independent contribution of maternal vitamin D observed in our study highlights its potential role as a modifiable prenatal factor. Early pregnancy may represent a particularly critical period because major neurodevelopmental events, including neuronal proliferation and migration, occur during the first and second trimesters [2].

The odds of developmental delay were more than five times higher in the deficient group compared with infants whose mothers had sufficient vitamin D levels. Comparable observations have been reported in longitudinal studies examining neurobehavioral and cognitive outcomes among children exposed to inadequate prenatal vitamin D concentrations [9, 10]. Although causality cannot be definitively established from observational studies, the consistency of findings across diverse populations lends support to a potentially meaningful relationship.

CONCLUSION

The study findings demonstrated a significant association between maternal vitamin D status during early pregnancy and infant neurodevelopmental outcomes at 12 months of age. Infants born to mothers with adequate vitamin D levels achieved higher cognitive, language, and motor scores on the Bayley-III assessment compared with those born to vitamin D deficient mothers. Maternal vitamin D concentration remained an independent predictor of cognitive development after adjusting for relevant confounding factors. These findings highlight the potential importance of maintaining optimal

vitamin D status during pregnancy. Early identification and correction of vitamin D deficiency may contribute to improved neurodevelopmental outcomes in children.

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