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Original Research Article

ASSOCIATION BETWEEN MATERNAL MICRONUTRIENT DEFICIENCIES AND INFANT NEURODEVELOPMENTAL OUTCOMES: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Maternal micronutrient deficiencies during pregnancy are highly prevalent in developing countries and may adversely affect fetal growth and neurodevelopment. Iron, vitamin D, and vitamin B12 are essential for neuronal maturation, myelination, and cognitive development. However, limited prospective studies have evaluated their combined influence on infant neurodevelopmental outcomes. This study was designed to assess the association between maternal deficiencies of iron, vitamin D, and vitamin B12 and infant neurodevelopmental outcomes.
Materials and Methods: A total of 138 pregnant women recruited during the first and second trimesters. Maternal serum ferritin, 25-hydroxyvitamin D, and vitamin B12 levels were estimated. Infants were followed up to 12 months of age. Neurodevelopment was assessed using the Bayley Scales of Infant Development, and growth parameters were evaluated using WHO Z-scores. Birth outcomes and NICU admissions were also recorded. Multivariable regression analysis was performed after adjusting for confounding variables.
Results: Iron deficiency was observed in 52.2% of mothers, followed by vitamin D deficiency (46.4%) and vitamin B12 deficiency (38.4%). Infants born to deficient mothers had significantly lower cognitive, language, and motor scores compared to infants of non-deficient mothers ($p<0.05$). Iron deficiency demonstrated the strongest association with cognitive impairment, while vitamin B12 deficiency predominantly affected language development. Multiple deficiencies were associated with poorer growth outcomes and higher NICU admissions.
Conclusion: Maternal micronutrient deficiencies significantly influence infant growth and neurodevelopment. Early antenatal nutritional screening and timely supplementation may improve long-term child health outcomes.
Keywords: Maternal nutrition, Iron deficiency, Vitamin D, Vitamin B12, Neurodevelopment, Infant growth, Pregnancy, Micronutrients.

INTRODUCTION

Maternal nutrition during pregnancy is a critical determinant of foetal growth and neurodevelopment. Adequate availability of micronutrients such as iron, vitamin D, and vitamin B12 is essential for normal brain maturation, neuronal differentiation, neurotransmitter synthesis, and myelination. Deficiencies of these micronutrients are highly prevalent among pregnant women in developing countries and continue to represent a major public health challenge.[1-3]

Iron plays an important role in oxygen transport, energy metabolism, and development of the central nervous system. Maternal iron deficiency during pregnancy has been associated with impaired cognitive, motor, and behavioral development in children.[4] Inadequate foetal iron supply during critical periods of brain growth may result in long-term neurodevelopmental deficits.[5]

Vitamin B12 is necessary for DNA synthesis and maintenance of neuronal myelin integrity. Deficiency during pregnancy may interfere with foetal neuronal maturation and synaptic development, leading to delayed language and cognitive functions in infants.[6] Several studies have demonstrated significant associations between low maternal vitamin B12 levels and adverse neurodevelopmental outcomes in early childhood.[7]
Vitamin D has emerged as an important neuroactive hormone involved in neuronal differentiation, neuroprotection, and regulation of neurotrophic factors. Maternal vitamin D deficiency has been linked with impaired neurodevelopment, language delay, and cognitive dysfunction in offspring.[8]
In India, micronutrient deficiencies frequently coexist because of poor dietary intake, socioeconomic deprivation, and increased nutritional demands during pregnancy. Although previous studies have evaluated the independent effects of iron, vitamin D, or vitamin B12 deficiency, limited prospective studies have examined their combined influence on infant neurodevelopment and growth outcomes.[9,10]
Therefore, the present prospective cohort study was conducted at MNR Medical College and Hospital to evaluate the association between maternal deficiencies of iron, vitamin D, and vitamin B12 and infant neurodevelopmental outcomes assessed using the Bayley Scales of Infant Development. The study also assessed the impact of maternal micronutrient status on birth outcomes and infant growth during early infancy.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Departments of Pediatrics and Department of Obstetrics & Gynaecology at MNR Medical College and Hospital, Sangareddy from January 2025 to March 2026. A total of 138 pregnant women attending the antenatal outpatient department of the OBG department were recruited.

Inclusion Criteria

Pregnant women aged 18-35 years, singleton pregnancy, gestational age ≤24 weeks at enrolment which was confirmed by ultrasound or last menstrual period, and willing to participate and agreed to attend follow-up schedules.

Exclusion Criteria

Pre-existing chronic illnesses, diabetes mellitus, hypertension, renal disease, thyroid disorders or neurological illness, multiple gestation, history of congenital foetal anomalies detected antenatally, severe pregnancy complications requiring early termination, not willing to participate and inability to complete follow-up.
Written informed consent was obtained from all participants after detailed explanation of study procedures. The study protocol was reviewed and approved by the Institutional Ethics Committee.
A detailed baseline information was obtained from all study participants using a structured proforma such as sociodemographic variables, obstetric history, BMI, dietary history and supplement use. A 5-7ml of venous blood samples were collected under aseptic conditions during enrolment by experience phlebotomists to assess haemoglobin (Hb) estimation, serum ferritin, serum 25-hydroxyvitamin, serum vitamin B12, serum calcium and parathyroid hormone (PTH). At delivery, cord blood samples were collected to measure neonatal levels of 25(OH)D, vitamin B12 and ferritin. All biochemical analyses were performed in the central laboratory using standardized methods with internal quality control.
At the time of delivery, the following neonatal parameters were recorded including birth weight, gestational age, mode of delivery, APGAR Score, and requirement for resuscitation. Infants were followed up at birth, at 6 months and at 12 months. Parents were contacted and reminded to ensure compliance with follow-up visits.
Anthropometric measurements such as weight, length, head circumference were measured at each follow-up visit and Growth indices were calculated using WHO Child Growth Standards. Infant neurodevelopment was assessed at 12 months using the Bayley Scales of Infant Development, a validated and widely used developmental assessment tool to assess the domains such as cognitive, language and motor development. Assessment was conducted by trained paediatricians or psychologists who were blinded to maternal micronutrient status to reduce observer bias.
Statistical Analysis: The collected data was analysed by using SPSS v.26.0. Descriptive Statistics was used to analyse continuous and categorical variables which represented in mean, standard deviation and frequency and percentages respectively. Independent t test was used for comparison of continuous variables and chi-square test for categorical variables. Multivariable regression models were constructed to assess the independent association between maternal micronutrient deficiencies and infant neurodevelopmental outcomes. A p-value of <0.05 was considered statistically significant.

Table 1: Demographic and clinical profile of study participants

Demographic/clinical Variable	Total cases (n=138)
	Mean±SD
Age (In years)	24.8 ± 3.6
BMI (kg/m²)	22.6 ± 2.8
Parity	
Primigravida	62 (44.9%)

Multigravida	76 (55.1%)
Socioeconomic status	
Lower socioeconomic status	83 (60.1%)
Educational status	
Primary education	13 (9.42%)
Secondary education	91 (65.9%)
Graduation & above	24 (17.4%)
Illiterate	10 (7.24%)

Table 2: Prevalence of deficiencies and combined deficiencies.

Micronutrient	Deficient	Normal
	Frequency (%)	Frequency (%)
Iron deficiency	72 (52.2%)	66 (47.8%)
Vitamin D deficiency	64 (46.4%)	74 (53.6%)
Vitamin B12 deficiency	53 (38.4%)	85 (61.6%)
Combined deficiencies		
No deficiency	32 (23.2%)	
Single deficiency	41 (29.7%)	
Two deficiencies	39 (28.3%)	
All three deficiencies	26 (18.8%)	

Table 3: Details of birth outcomes

Outcome	Deficient	Non-deficient	p-value
	Mean±SD	Mean±SD	
Birth Outcomes by Micronutrient Status			
Low birth weight (<2.5 kg)	34.6%	18.2%	0.02
Preterm birth	16.9%	9.1%	0.11
NICU admission	27.7%	13.6%	0.03
APGAR score			
At 1 min	6.8 ± 1.2	7.5 ± 1.0	0.01
At 5 min	8.1 ± 0.9	8.7 ± 0.7	0.02
Growth Parameters at 12 Months (WHO Z-Scores)			
Weight-for-age (WAZ)	−1.25 ± 0.9	−0.62 ± 0.7	0.001
Length-for-age (LAZ)	−1.38 ± 0.8	−0.70 ± 0.6	0.001
Head circumference	−1.12 ± 0.7	−0.58 ± 0.5	0.002

Table 4: Neurodevelopmental outcomes assessed by Bayley scales of infant development

Domain	Deficient	Non-deficient	Mean Difference	p-value
Cognitive	85.4 ± 7.2	92.1 ± 6.8	-6.7	0.001
Language	83.7 ± 8.1	90.5 ± 7.3	-6.8	0.001
Motor	86.2 ± 6.5	91.3 ± 6.1	-5.1	0.002

Table 5: Micronutrient specific effects on infant neurodevelopmental domains.

Micronutrient Deficiency	Level of impact		
	Cognitive domain	Language domain	Motor domain
Iron deficiency	Severe	Moderate	Severe
Vitamin-B12 deficiency	Moderate	Severe	Mild
Vitamin-D deficiency	Mild to moderate	Mild	Mild

Table 6: Multivariable Regression Analysis after adjusting for demographic variables.

Predictor	Outcome	β	95% CI	p-value
Iron deficiency	Cognitive	−0.42	−0.58 to −0.26	<0.001
Vitamin B12 deficiency	Language	−0.31	−0.52 to −0.10	0.01
Vitamin D deficiency	Composite	−0.25	−0.44 to −0.06	0.03

DISCUSSION

The present prospective cohort study evaluated the association between maternal micronutrient deficiencies, particularly iron, vitamin D, and vitamin B12, and infant neurodevelopmental outcomes among mother infant dyads attending Department of OBG at MNR Medical College and Hospital. A high prevalence of maternal micronutrient deficiencies was observed in the present study, with iron deficiency affecting more than half of the participants, followed by vitamin D and vitamin B12 deficiencies. This finding is consistent with the nutritional burden reported among pregnant women in low and middle-income countries, particularly in India, where dietary inadequacy and socioeconomic limitations contribute substantially to maternal undernutrition. Previous evidence has demonstrated that maternal nutritional status during pregnancy is a critical determinant of foetal brain development and long-term neurocognitive outcomes in offspring.[11,12] The present study identified a significant association between maternal iron deficiency and reduced infant cognitive and motor scores. Iron deficiency emerged as the strongest predictor of impaired neurodevelopment in multivariable regression analysis. Iron is essential for neuronal metabolism, neurotransmitter synthesis, myelination, and hippocampal development. During foetal life, rapid brain growth requires adequate iron availability, and deficiency during this critical developmental period may result in long-lasting neurodevelopmental impairment. Similar observations were reported in several cohort studies demonstrating that foetal iron deprivation may impair memory, attention, and psychomotor development.[12] A systematic review by Quezada-Pinedo et al. reported that maternal iron deficiency during pregnancy was associated with poorer cognitive and behavioral outcomes in children.[13] The strong dose response relationship observed in the present study, where worsening anemia severity corresponded with progressively lower cognitive scores, further supports the biological plausibility of this association.

In addition to neurodevelopmental impairment, maternal iron deficiency was associated with lower birth weight and increased NICU admissions in the current study. Iron deficiency can compromise placental oxygen transport and foetal growth, thereby increasing the risk of intrauterine growth restriction and adverse neonatal adaptation. Lower Apgar scores among infants born to deficient mothers in the present study may reflect impaired foetal reserve and compromised perinatal transition. Similar findings have been documented in studies from South Asia, where maternal anemia was associated with low birth weight, preterm birth, and neonatal morbidity.[14]

Vitamin B12 deficiency demonstrated a significant association with language delay and moderate cognitive impairment in the present study. Vitamin B12 plays an essential role in DNA synthesis, methylation reactions, and myelination of the central nervous system. Deficiency during pregnancy can interfere with neuronal maturation and synaptic connectivity, thereby affecting early neurodevelopment. The findings of the current study are supported by the ECLIPSES cohort study, which reported that adequate maternal vitamin B12 levels during early pregnancy were associated with better infant motor, language, and cognitive performance assessed using the Bayley Scales of Infant Development.[15]

Similarly, Cruz-Rodríguez et al. observed that infants born to mothers with sufficient vitamin B12 concentrations had significantly higher receptive language and motor scores during infancy.[15] Evidence from recent reviews also suggests that maternal vitamin B12 deficiency may contribute to developmental delay, reduced cognitive performance, and neuropsychiatric disorders in offspring.[16] Although some studies have shown inconsistent findings regarding long-term neurodevelopmental outcomes, the majority of prospective studies indicate that low maternal vitamin B12 status adversely affects infant brain development, especially when deficiency occurs during early gestation.

Vitamin D deficiency in the present study demonstrated mild to moderate but statistically significant associations with overall neurodevelopmental performance. Vitamin D receptors are widely distributed in the foetal brain, and vitamin D is involved in neuronal differentiation, axonal connectivity, neuroprotection, and regulation of neurotrophic factors. Deficiency during pregnancy may therefore impair foetal brain maturation and subsequent developmental outcomes. Previous literature has highlighted the importance of maternal vitamin D in neurodevelopmental programming.[17,18[Although the effect size observed in the present study was lower compared to iron deficiency, vitamin D deficiency remained an independent predictor even after adjustment for confounders. The comparatively smaller effect may be related to the multifactorial nature of vitamin D metabolism and variability in sunlight exposure, dietary intake, and supplementation practices.

One of the important findings of the present study was the coexistence of multiple micronutrient deficiencies among a large proportion of participants. Nearly half of the mothers had two or more deficiencies, and infants born to these mothers demonstrated the poorest developmental outcomes. This finding emphasizes the synergistic effect of nutritional inadequacies during foetal development. Maternal nutritional deficiencies rarely occur in isolation, particularly in resource limited settings. The coexistence of iron, vitamin D, and vitamin B12 deficiencies may exert additive adverse effects on neuronal development, myelination, and synaptic function. Similar observations have been reported in reviews evaluating maternal nutrition and offspring cognition, where combined nutritional deficiencies were associated with greater developmental compromise than isolated deficiencies.[12,19]

The present study also demonstrated significant growth faltering among infants exposed to maternal micronutrient deficiencies. Weight for age, length for age, and head circumference Z scores were significantly lower among infants of deficient mothers. Nutritional deficiencies during pregnancy can impair placental growth, foetal nutrient transfer, and postnatal metabolic adaptation, thereby influencing both somatic and neurodevelopmental growth. Reduced head circumference observed in the present study may indicate suboptimal brain growth during early infancy. Similar associations between maternal nutritional inadequacy and impaired child growth have been reported previously.[11,[12).]

In terms of limitations, study was conducted at a single tertiary care center, which may limit generalizability to other populations. Follow up was limited to 12 months of age, and longer-term neurodevelopmental assessment may provide a better understanding of persistent developmental effects. Additionally, dietary intake assessment was based partly on self-reporting and may be subject to recall bias. Despite these limitations, the findings have important public health implications. India continues to experience a high burden of maternal anemia and micronutrient deficiencies, especially among socioeconomically disadvantaged populations. Early identification and correction of micronutrient deficiencies during pregnancy may represent a cost-effective strategy to improve infant neurodevelopmental outcomes and reduce long term cognitive impairment.

CONCLUSION

Maternal deficiencies of iron, vitamin D, and vitamin B12 during pregnancy were significantly associated with impaired infant neurodevelopment and growth outcomes. Iron deficiency demonstrated the strongest effect on cognitive development, while vitamin B12 deficiency predominantly affected language skills. Multiple micronutrient deficiencies further worsened developmental outcomes. Early antenatal nutritional screening and appropriate supplementation are essential to improve foetal brain development, reduce adverse neonatal outcomes, and promote optimal child growth and neurodevelopment.

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