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ORIGINAL RESEARCH ARTICLE

Association of Maternal Anemia Severity with Neurodevelopmental Outcomes in Infants: A Prospective Cohort Study from Central India

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Abstract

Background. Maternal anemia is common during pregnancy and may be associated with adverse perinatal and developmental outcomes. Iron deficiency is an important contributor to maternal anemia and may affect fetal brain development through effects on myelination, synaptogenesis, hippocampal neurogenesis, mitochondrial energy metabolism, and neurotransmitter synthesis. Evidence examining early neurodevelopmental outcomes according to maternal anemia severity, particularly during the first six months of life, remains limited. **Objectives.** To assess the association between maternal anemia severity and neurodevelopmental outcomes of infants at six months of age using the Denver Developmental Screening Test-II (DDST-II). **Methods.** A prospective cohort study was conducted at Rani Durgawati (Elgin) Hospital, Jabalpur, Madhya Pradesh (N = 168 enrolled mother–infant dyads). The severe-anemia group comprised 80 mothers (Hb <7 g/dL), and the moderate-anemia group comprised 88 mothers (Hb 7.0–9.9 g/dL). Although assessments were planned at 1, 2, 3, 4–5, and 6 months, only six-month developmental assessment data were available in a form suitable for the present comparative analysis. Intermediate records were insufficient for analysis. Group comparisons used the independent-samples t-test and chi-square or Fisher's exact test, as appropriate. **Results.** Mean maternal haemoglobin was 5.22 ± 0.71 g/dL in the severe-anemia group compared with 8.81 ± 0.79 g/dL in the moderate-anemia group ($p < 0.0001$). Mean birth weight was significantly lower in the severe-anemia group (2,337 ± 87 g) than in the moderate-anemia group (2,835 ± 248 g) ($p < 0.0001$). At six months, gross motor milestones were achieved by 100% of infants in both groups. Caution responses were uncommon, and no developmental delay was recorded in any domain. None of the four DDST-II domains showed a statistically significant intergroup difference. **Conclusion.** In this cohort comparing infants born to mothers with severe versus moderate anemia, no statistically significant differences were observed in the reported DDST-II domain outcomes at six months. Because developmental Delay events were absent, Caution observations were sparse, and follow-up data suitable for analysis were limited to six months, these findings do not establish equivalence or exclude later developmental differences. The reported concentration of low birth weight in the severe-anemia group requires confirmation against the original study records before firm interpretation.

Keywords: Maternal anaemia, anaemia severity, neurodevelopmental outcomes, DDST-II, infant, low birth weight, India.

Key Points

- A prospective cohort of 168 mother–infant dyads compared six-month outcomes in infants born to mothers with severe or moderate anemia.
- Mean birth weight was lower in the severe-anemia group than in the moderate-anemia group (2,337 ± 87 g vs 2,835 ± 248 g; $p < 0.0001$).
- No statistically significant differences were observed between groups across the four DDST-II developmental domains at six months, and no developmental delay was recorded.
- Gross motor milestones were achieved by all infants; sparse caution responses and limited follow-up mean later developmental differences cannot be excluded.

Introduction

Anemia in pregnancy remains one of the most prevalent nutritional disorders globally, affecting an estimated 36% of pregnant women worldwide and contributing to over 115,000 maternal deaths annually. [1] Iron deficiency anemia (IDA) accounts for approximately 50% of all cases and is particularly concentrated in low- and middle-income countries (LMICs), where poverty, vegetarian dietary patterns, and inadequate antenatal care contribute to the burden. [2]

India bears a disproportionate burden. The National Family Health Survey-5 (NFHS-5, 2019–21) estimates that 52.2% of pregnant Indian women are anaemic, with Madhya Pradesh recording a prevalence exceeding 54.7%. [3] Rani Durgawati (Elgin) Civil Hospital Jabalpur serves an obstetric population drawn from Jabalpur and surrounding rural and socioeconomically underserved areas, including tribal districts, where maternal anemia may be compounded by dietary practices, high parity, and suboptimal compliance with iron and folic acid (IFA) supplementation. [4]

Iron is not merely a haematological nutrient but an obligatory cofactor for several processes critical to fetal brain development. It is essential for myelination via its role in oligodendrocyte maturation and myelin protein gene expression synaptogenesis, hippocampal neurogenesis, mitochondrial energy metabolism, and the synthesis of monoamine neurotransmitters including dopamine and serotonin. [5,6] These processes reach their peak intensity during the third trimester and the first postnatal months, establishing this period as the most critical and vulnerable window for nutritional influence on brain architecture. [7]

Evidence from studies of prenatal iron deficiency and maternal anemia suggests possible associations with offspring neurodevelopment, although the populations, exposure definitions, ages at assessment, and outcomes vary across studies. Auditory brainstem response (ABR) studies have reported prolonged latencies in neonates born to mothers with iron deficiency anemia. [9] Longitudinal work by Lozoff and colleagues has described developmental and behavioral differences associated with early-life iron deficiency at later ages. [10] A Swedish registry-based cohort study reported associations between prenatal maternal anemia and selected neurodevelopmental disorders in offspring. [8]

Despite this body of evidence, the preponderance of published studies have assessed neurodevelopmental outcomes at 12 months of age or later, and the majority originate from Latin American, African, or East Asian cohorts. Prospective data examining the earliest neurodevelopmental trajectory from birth to six months in infants of severely anemic Indian mothers are virtually absent from the published literature. Early infancy represents the most plastic and simultaneously most vulnerable period for brain development. Identifying neurodevelopmental compromise at this stage could enable timely preventive and therapeutic interventions within routine antenatal and postnatal care frameworks.

The present study was therefore designed to prospectively assess the association between maternal anemia severity and neurodevelopmental outcomes of infants at six months of age in a hospital serving a predominantly rural and socioeconomically underserved catchment area in Jabalpur, Madhya Pradesh, using the Denver Developmental Screening Test-II (DDST-II) across four developmental domains. Because both cohorts comprised mothers with anemia, the study specifically compared infants born to mothers with severe anemia with those born to mothers with moderate anemia.

Materials and Methods

2.1 Study Design and Setting

This prospective cohort study was conducted at the Rani Durgawati (Elgin) Civil Hospital for Women, Jabalpur, Madhya Pradesh - a secondary government hospital serving as an institutional delivery facility for Jabalpur City and surrounding rural and socioeconomically underserved areas. Developmental follow-up assessments were conducted at the SNCU follow-up clinic. The mothers who delivered during July 2025 – Dec 2025 were enrolled in this study who have reporting for their routine vaccination at Rani Durgawati (Elgin) Civil Hospital for Women, Jabalpur and were followed prospectively with infant developmental assessments through six months of age.

2.2 Study Population

The source population comprised pregnant women in the third trimester registered for institutional delivery at Elgin Hospital during the enrolment period. Two cohorts were constituted from this population: an exposed cohort (severe anaemia, S) consisting of mothers with documented haemoglobin (Hb) <7 g/dL and a comparison cohort (moderate anaemia, M) consisting of mothers with Hb 7.0–9.9 g/dL, both measured in the third trimester and recorded in the hospital's electronic antenatal database (cyanmethaemoglobin method).

2.3 Eligibility Criteria

Inclusion criteria: singleton, full-term (≥37 completed weeks) live birth; exclusively breastfed infant; documented third-trimester maternal hemoglobin; and written informed consent.

Exclusion criteria: maternal haemoglobinopathies (sickle cell disease, thalassaemia); chronic maternal illness (diabetes mellitus, hypertension, thyroid disease, asthma); third-trimester blood transfusion or parenteral iron sucrose; preterm infants (<37 weeks); major congenital anomalies; neonatal birth asphyxia or prolonged NICU admission; non-exclusively breastfed infants.

2.4 Sample Size

Sample size was calculated using the two-cohort proportion formula ($\alpha = 0.05$, power = 80%), assuming a developmental delay proportion of 35% in the exposed cohort and 15% in the comparison cohort, yielding a minimum of 70 per group. Allowing 10% loss to follow-up, approximately 77–80 dyads per cohort were required. Total population sampling over the six-month enrolment period was adopted, yielding N = 168 dyads (S: 80; M: 88).

2.5 Data Collection

Assessments were planned at 1 month, 2 months, 3 months, 4–5 months, and 6 months of age. Only the six-month developmental assessment records were available in a form suitable for the present comparative analysis; intermediate records were not sufficiently documented for analysis because of practical resource and follow-up limitations. Baseline maternal data listed in the study records included age, parity, educational status, dietary pattern, and IFA supplementation regularity. Family income was listed in the original data-collection description, but its was found unsuitable and completeness for reporting and analysis purpose. Neonatal data included birth weight, gestational age, sex, mode of delivery, and perinatal complications. Breastfeeding status was intended to be confirmed at six month followup. Haemoglobin classification followed the cited WHO criteria. [11]

2.6 Neurodevelopmental Assessment

The Denver Developmental Screening Test-II (DDST-II) was used to screen four developmental domains: Personal–Social, Fine Motor–Adaptive, Language, and Gross Motor. Domain-level observations were classified as Achieved (A), Caution (C), or Delay (D) according to the instrument's age-referenced scoring rules. These

categories describe screening performance and are not, by themselves, a diagnosis of a developmental disorder. The results presented here are domain-specific; a separate overall screening classification is not reported because a verifiable overall classification was not available in the supplied analysis. Assessors were blinded to maternal anaemia group assignment. [12,13]

2.7 Statistical Analysis

Data were analysed using SPSS v25.0 (IBM Corporation, Armonk, NY). Continuous variables are expressed as mean ± SD. Group comparisons used the independent t-test for normally distributed continuous variables and the chi-square test or Fisher's exact test, as appropriate, for categorical variables. Because no developmental Delay events were observed and Caution events were sparse, multivariable modelling of developmental outcomes was not considered reliable. A two-tailed $p<0.05$ was considered statistically significant.

2.8 Ethical Approval

Approval from the Institutional Ethics Committee of NSCB Medical College, Jabalpur, was obtained prior to the commencement of the study (Ref. No. IEC/2026/3131 dated 06/04/2026, based on the NSCB IEC meeting held on 21/02/2026). Written informed consent was obtained from all participants. Infants identified with developmental concerns were referred for appropriate intervention. All data were anonymized and stored securely.

Results

3.1 Baseline Maternal Characteristics

A total of 168 mother-infant dyads were enrolled: 80 in the severe anaemia group (S) and 88 in the moderate anaemia group (M). The majority of mothers (55.36%) were aged 20–25 years; 27.98% belonged to the 25–30-year age group. The distribution of maternal age across groups did not differ significantly ($\chi^2 = 3.76$, df = 4, p = 0.44). Secondary-level education predominated (72.62%). A vegetarian diet was followed by 70.24% of participants. Regular IFA supplementation was reported by 70.24%, while 29.76% were non-compliant (irregular or not taken). Multigravid women (gravida ≥2) constituted 78% of the cohort.

Mean maternal haemoglobin was significantly lower in the severe group (5.22 ± 0.71 g/dL) versus the moderate group (8.81 ± 0.79 g/dL; $p<0.0001$). The mean maternal age was 28.06 ± 5.69 years (S) and 26.99 ± 5.25 years (M), with no statistically significant intergroup difference ($p>0.05$).

3.2 Perinatal Outcomes

A clinically important finding was that all 80 low birth weight infants (birth weight <2,500 g) belonged to the severe-anemia group (100% of S group; 0% of M group), representing 47.62% of the total cohort. Mean birth weight in the S group was 2,337 ± 87 g, compared with 2,835 ± 248 g in the M group ($p<0.0001$). Mode of delivery (LSCS: 51.1% vs 51.2%; $p > 0.05$) and infant sex distribution (male: 53.8% vs 54.5%; $p > 0.05$) were comparable between groups.

3.3 Neurodevelopmental Outcomes at 6 Months (DDST-II)

Overall developmental achievement rates were high across all four DDST-II domains. The results of cross-tabulation analyses are presented in Table 2. The primary comparative analysis was based on the six-month assessment.

The gross motor domain showed 100% achievement in both groups with zero Caution or Delay. The language domain demonstrated the highest proportion of Caution responses, with 4.5% in the Moderate group compared with 1.2% in the Severe group (Fisher's exact p = 0.370). No Delay was recorded in any domain in either cohort. None of the four developmental domains showed a statistically significant intergroup difference.

Discussion

The present study compared six-month DDST-II domain outcomes among infants born to mothers with severe versus moderate anemia. No statistically significant differences were reported across the four domains. Because both cohorts comprised mothers with anemia, the findings compare outcomes by anemia severity rather than estimate developmental risk attributable to maternal anemia compared with a non-anemic population.

Our results showed statistically insignificant differences at six months and thus cannot describe developmental trajectories across infancy. Developmental differences related to prenatal nutritional exposures may become more apparent later in childhood, and DDST-II may not detect subtle differences in early infancy. Tran et al. [14], in a prospective cohort from rural Vietnam, reported an association between maternal iron deficiency anemia and child development using more comprehensive developmental assessment. The present study did not detect significant domain-level differences, which may reflect the small number of Caution observations and the limited sensitivity of DDST-II compared with the Bayley Scales for detecting subtle developmental differences in early infancy.

The Language domain showed the closest trend toward intergroup differentiation (Moderate Caution 4.5% vs Severe 1.2%; Fisher's exact p = 0.370) and the observation were comparable between both the groups, because the absolute number of Caution cases was small. Studies by ElAlfy et al. [9] using auditory brainstem responses demonstrated prolonged ABR latencies in neonates of iron-deficient mothers, providing biological context for possible auditory pathway effects. The difference observed in the present study may reflect sampling variability and requires confirmation in larger prospective studies.

The LBW finding is among the important perinatal observations of this study. The reported concentration of all 80 LBW infants in the Severe anemia group (mean birth weight: 2,337 vs 2,835 g; $p<0.0001$). Low birth weight is independently associated with adverse developmental outcomes in many populations. [16]

The Gross Motor domain demonstrated 100% achievement in both groups. Given the absence of Caution or Delay events in this domain, and both were statistical comparable having insignificant differences.

The Swedish registry study by Wiegersma et al. [8] reported associations between prenatal maternal anemia

Table 1. Baseline maternal and neonatal characteristics by anemia group (N = 168)

Characteristic	Severe (S, n=80)	Moderate (M, n=88)	p-value
Mean Age (years)	28.06 ± 5.69	26.99 ± 5.25	0.194
Mean Hb (g/dL)	5.22 ± 0.71	8.81 ± 0.79	<0.001
Mean Birth Weight (g)	2337 ± 87	2835 ± 248	<0.001
Vegetarian diet, n (%)	52 (65.0%)	66 (75.0%)	0.152
Regular IFA, n (%)	52 (65.0%)	66 (75.0%)	0.152
Multigravid (G ≥ 2, n (%)	62 (77.5%)	69 (78.4%)	0.885
LSCS, n (%)	41 (51.2%)	45 (51.1%)	1.000
Male infant, n (%)	43 (53.8%)	48 (54.5%)	1.000
LBW (<2500 g) (n)	80 (100.0%)	0 (0.0%)	<0.001

Percentages are calculated using the group denominators shown in the table; Hb = haemoglobin; IFA = iron and folic acid; LSCS = lower-segment caesarean section; LBW = low birth weight.

Table 2. DDST-II developmental domain outcomes by anemia group at 6 months of age

Domain	Outcome	Severe (S) n=80	Moderate (M): n=88	Statistical test	p-value
Personal–Social	Achieved (A)	77 (96.2%)	85 (96.6%)	Fisher's exact	P>0.05
	Caution (C)	3 (3.8%)	3 (3.4%)		
	Delay (D)	0 (0.0%)	0 (0.0%)		
Fine Motor–Adaptive	Achieved (A)	79 (98.8%)	87 (98.9%)	Fisher's exact	P>0.05
	Caution (C)	1 (1.2%)	1 (1.1%)		
	Delay (D)	0 (0.0%)	0 (0.0%)		
Language	Achieved (A)	79 (98.8%)	84 (95.5%)	Fisher's exact	P>0.05
	Caution (C)	1 (1.2%)	4 (4.5%)		
	Delay (D)	0 (0.0%)	0 (0.0%)		
Gross Motor	Achieved (A)	80 (100.0%)	88 (100.0%)	Fisher's exact not applicable	
	Caution (C)	0 (0.0%)	0 (0.0%)		
	Delay (D)	0 (0.0%)	0 (0.0%)		

DDST-II = Denver Developmental Screening Test-II; A = Achieved; C = Caution; D = Delay. Fisher's exact test was used for sparse categorical comparisons; the Gross Motor comparison was not statistically estimable because all observations were Achieved.

and selected neurodevelopmental disorders assessed later in childhood. These findings reinforce the limitation of restricting the present assessment to six months. Lozoff et al. [10] also described longer-term developmental and behavioral differences associated with early-life iron deficiency.

The reported cohort had high proportions of vegetarian dietary practice and multigravidity, and regular IFA supplementation was reported by 70.24%. The hospital serves a rural and socioeconomically underserved catchment area, including adjoining districts with substantial tribal populations; however, participant-level tribal status was not recorded in a form permitting reliable classification. Family-income data and their completeness were underreported hence were dropped and socioeconomic findings were not available to present.

Strengths

This study prospectively compared six-month DDST-II domain outcomes in an institutional obstetric population in central India. Use of a standardized screening instrument and blinded assessment, as described in the study records, are strengths. The absence of analyzable intermediate assessments, however, means that serial developmental trajectories cannot be evaluated in the present report.

Limitations

The study has several limitations. First, only six-month developmental assessment data were available in a form suitable for the present comparative analysis; intermediate follow-up records were insufficient for analysis, limiting assessment of developmental trajectories. Second, DDST-II is a screening instrument and may not detect subtle neurocognitive differences identifiable through more comprehensive assessment. Third, both groups comprised mothers with anemia and there was no non-anemic control group. Fourth, no developmental Delay events were observed and Caution responses were sparse, limiting statistical power and making multivariable outcome modelling unreliable. Fifth, biochemical markers confirming iron deficiency were not undertaken due to limited resource setting, so the findings concern maternal anemia severity rather than confirmed iron deficiency anemia. Individual participant tribal status was not recorded in a form permitting reliable classification, and family-income data were also not recorded. Finally, the single-institution sample limits generalisability to community settings.

Conclusion

In this cohort comparing infants born to mothers with severe versus moderate anemia, no statistically significant differences were reported in DDST-II domain outcomes at six months. The absence of developmental Delay events, sparse Caution observations, and lack of analyzable intermediate assessments limit conclusions about longer-term neurodevelopment. The reported concentration of low birth weight in the severe-anemia group should not be interpreted definitively until the original records and eligibility criteria have been reconciled. Larger prospective studies with longer follow-up and comprehensive assessment of maternal iron status and infant development are warranted. Based on the results obtained in the present study, following points are recommended:

1. Universal third-trimester haemoglobin screening with appropriate treatment and follow-up for moderate-to-severe maternal anemia within government antenatal care programmes.
2. Intensification of dietary iron counselling, particularly for vegetarian women in rural and underserved communities, incorporating iron absorption enhancers such as vitamin C-rich foods and avoidance of inhibitors.
3. Serial DDST-II developmental surveillance at 6, 12, 18, and 24 months for infants born to mothers with moderate-to-severe anemia, particularly those with low

birth weight.
4. Longitudinal follow-up of the present cohort at 12, 18, and 24 months of age to detect later neurodevelopmental differences associated with maternal anemia severity.
5. Larger, multi-centre prospective cohort studies with comprehensive maternal iron-status profiling and use of both DDST-II and more comprehensive developmental assessments such as the Bayley Scales are needed to generate stronger evidence for Indian policy-making.

Declarations

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Generative Ai (Claude ai) to improve language and readability. After using this tool, the authors thoroughly reviewed and edited the content as needed and took full responsibility for the final content of the publication.

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Conflict of interest

The authors declare no conflict of interest.

Ethics approval

Ethical clearance was obtained from the Institutional Ethics Committee, NSCB Medical College, Jabalpur, (Ref. No. IEC/2026/3131 dated 06/04/2026 on the basis of NSCB IEC meeting held on 21/02/2026).

Consent to participate

Written informed consent was obtained from all participants. Infants identified with developmental concerns were referred for appropriate intervention. All data were anonymised and stored securely.

Consent for publication

Not applicable. This manuscript does not contain identifiable individual-level data or images.

Availability of data and material

The data used in this study are were collected during a postgraduate thesis submitted to the University of Kerala for the award of Postgraduate Diploma in Developmental Neurology. The data are available from the corresponding author, Dr Pallavi Londe, upon reasonable request.

Code availability

The data were analysed using SPSS and the scripts are available from the corresponding author upon reasonable request.

Authors' contributions

Pallavi Londe: Conceptualization, Methodology, Data curation, Formal analysis, Writing – review and editing. Arvind Kavishwar: Data analysis, Methodology, Writing – original manuscript draft, Writing – review and editing. Visharad Nandanwar: Data curation, Data collation and Formal analysis. Monica Lazarus: Supervision, Formal analysis, Writing – review and editing, and Pradeep Jain: Supervision and Methodology, Formal analysis.

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