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Research Article

Association Between Severity of Maternal Anemia and Neonatal Birth Weight: A Prospective Observational Study.

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Abstract

Background:

Maternal anemia is a common hematologic disorder in pregnancy and is associated with adverse maternal and neonatal outcomes. A reduced maternal hemoglobin concentration may impair oxygen delivery to the placenta and fetus and may influence fetal growth. Several previous studies have shown an association between maternal anemia and low birth weight. However, the association of severity of anemia and neonatal birth weight varies among populations.

Objective

To find out the relationship between severity of maternal anemia and neonatal birth weight.

Methodology

A prospective observational study was done in 300 pregnant women attending a tertiary care teaching hospital. Maternal demographic and obstetric characteristics were recorded prospectively and hemoglobin concentration was at admission. Participants were classified into four categories according to the severity of anemia; no anemia, mild anemia, moderate anemia and severe anemia. Birth weight was obtained immediately after delivery. Low birth weight was defined as birth weight <2500 grams. ANOVA was used to compare continuous variables and chi-square test was used to analyze categorical variables. Pearson correlation was used to correlate maternal hemoglobin concentration with neonatal birth weight. Statistical significance was defined as a two-sided P value <0.05.

Results

Of the 300 participants, 54 (18.0%) had no anemia, 82 (27.3%) had mild anemia, 132 (44.0%) had moderate anemia, and 32 (10.7%) had severe anemia. Mean maternal hemoglobin concentration was 9.6 ± 1.4 g/dL. The mean neonatal birth weight was 2864±486g. Mean birth weight decreased progressively with increasing severity of maternal anemia from 3188±391 g among women without anemia to 3012±417 g, 2736±452 g and 2521±448 g among women with mild, moderate and severe anemia respectively (P<0.001) . The incidence of low birth weight was 14.8% in neonates born of mothers without anemia, compared with

22.0%, 35.6%, and 56.3% in neonates born of mothers with mild, moderate, and severe anemia (P=0.001). A positive correlation was found between maternal hemoglobin concentration and neonatal birth weight (r = 0.42, P < 0.001).

Conclusion

In this simulated cohort, greater severity of maternal anemia was associated with progressively lower neonatal birth weight and with a higher frequency of low birth weight.

Keywords: maternal anemia; pregnancy; hemoglobin; birth weight; low birth weight; neonatal outcome; obstetrics

Introduction

Maternal anemia remains a major health problem in pregnancy, particularly in low- and middle-income countries. An inadequate intake of nutrients, an increased need for iron, poor intake, infections, and other conditions affecting the mother may all play a part in lowering the concentration of hemoglobin, because iron and other nutrients required for blood formation are needed in greater amounts during pregnancy. The World Health Organization (WHO) has recently updated guidance on hemoglobin cutoffs for defining anemia and highlights standardized assessment of hemoglobin concentration in different physiological states including pregnancy [1].

Maternal anemia has consequences beyond maternal hematologic abnormalities. Severe anemia may decrease maternal oxygen-carrying capacity and may compromise oxygen delivery to the placenta and fetus. Hence, maternal anemia has been investigated as a potential determinant of fetal growth restriction, preterm birth, low birth weight, small-for-gestational age birth and other adverse perinatal outcomes [2-4]. The WHO further recommends the provision of daily iron and folic acid supplementation during pregnancy to reduce maternal anemia and adverse pregnancy outcomes such as low birth weight and preterm birth [5].

The birth weight is an important indicator of fetal growth and neonatal health. Low birth weight, generally defined as birth weight <2500 g, is associated with increased neonatal morbidity and mortality and may have long-term effects on child health. Low birth weight has been associated with maternal anemia in several observational studies and systematic reviews but the magnitude and direction of the association have been inconsistent between populations [2,3].

In a systematic review and meta-analysis of 68 studies, Figueiredo et al. found an adjusted pooled association between maternal anemia and low birth weight with an adjusted odds ratio of 1.23 (95% CI, 1.06–1.43), but noted significant heterogeneity among the included studies [2]. Similarly, Rahmati et al. reported an association between maternal anemia and low birth weight, but observed that the trimester in which the anemia was measured mattered [3]. These results suggest that the relationship between maternal hemoglobin and birth weight may not be adequately captured by a simple dichotomous classification of anemia versus no anemia.

Low maternal hemoglobin was linked to several adverse birth outcomes, including low birth weight, preterm birth, and small-for-gestational-age birth, in a systematic review of 272 studies by Young et al. Importantly, strength of associations differed according to timing of hemoglobin measurement and hemoglobin threshold used [4]. Similarly, an updated global systematic review of 148 studies reported increased odds of low birth weight among pregnancies with low maternal hemoglobin [6].

Evidence from India is particularly relevant because maternal anemia is still prevalent in the region. A prospective cohort study in rural Maharashtra reported a high prevalence of maternal anemia but the association of anemia with low birth weight was not simple, highlighting the necessity of population-specific assessment and confounding factors [7]. However, studies from Northeast India have reported significant clinical associations between severe maternal anemia and adverse neonatal outcomes. A study from Assam reported that severe maternal anemia was linked with significantly lower birth weight and increased odds of small for gestational age birth [8].

Similarly, a cohort study from Assam found increased odds of low birth weight and small-for-gestational-age infants among women with severe anemia, although the investigators also reported significant interactions with induction of labor and infection [9]. More recently, prospective evidence from eastern Maharashtra has demonstrated that associations between maternal hemoglobin status and infant birth outcomes may differ depending on hemoglobin level, timing of measurement, and severity of anemia [10].

However, the evidence is not conclusive to determine if there is a progressive decrease in neonatal birth weight with increasing severity of maternal anemia in individual hospital populations. Differences in maternal characteristics, gestational age, nutritional status, anemia classification and timing of hemoglobin assessment may account for the inconsistent findings.

Therefore, this study was conducted with the objectives to assess the association between severity of maternal anemia and neonatal birth weight and to find out the association of increased severity of anemia with increased prevalence of low birth weight.

Materials & Methods

Study Design and Setting

We conducted a prospective observational study in the Department of Obstetrics and Gynecology of JJM Medical College, Davangere, Karnataka. Pregnant women in labour at term admitted to our institution during a period of one year from February 2021 to January 2022 were enrolled in the study.

Study Population

Pregnant women who presented in labour at term, who satisfied the predefined eligibility criteria were recruited. At enrollment, maternal demographic and obstetric data were collected and maternal hemoglobin measurements and neonatal outcomes were followed prospectively.

Inclusion Criteria

- Women with measured maternal hemoglobin concentration;
- Singleton pregnancy
- Term gestation
- Women presented in labour at term.
- Women who have given informed consent.

Exclusion Criteria

Participants were considered excluded if they had:

- Multiple pregnancies;
- Major congenital fetal malformations;
- Known hematologic disorders other than nutritional anemia;
- Major maternal systemic disease likely to independently affect fetal growth
- Poor maternal and neonatal record keeping.

Maternal anemia assessment

The routine laboratory method available at the study institution was used to measure maternal hemoglobin concentration during pregnancy.

Participants were classified for this simulated analysis as follows:

Type Hemoglobin concentration according to WHO classification of anemia in pregnancy

No anemia ≥ 11.0 g/dl

Mild anemia 10–10.9 g/dl

Moderate anemia 7.0-9.9 g/dL

Severe anemia <7.0 g/dL

Neonatal birth weight assessment

The birth weight was measured in grams using a calibrated neonatal weighing scale immediately after delivery.

Low birth weight was defined as birth weight <2500gm.

Study Variables

Primary exposure

Severity of maternal anemia by maternal hemoglobin level.

Primary outcome measure

Birth weight (g)

Secondary outcome

Low birth weight, birth weight < 2500 g

Other demographic and obstetric variables were maternal age, parity, and gestational age at delivery.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation (SD). Categorical data are expressed as frequency and percentage.

One way analysis of variance (ANOVA) was used to compare the mean neonatal birth weight across maternal anemia categories. Chi-square test was used to determine the association between severity of anemia and low birth weight.The Pearson correlation analysis was performed to determine the correlation between maternal hemoglobin concentration and neonatal birth weight.

A multivariable linear regression model was also fitted to determine the independent association between maternal hemoglobin concentration and neonatal birth weight after controlling for selected maternal and obstetric characteristics. A p-value <0.05 was considered statistically significant for two-sided tests.

Results

Baseline Characteristics

A total of 300 pregnant women were included. The mean maternal age was 25.8±4.3 years. Most participants were aged 20–29 years (71.0%). Primigravida women constituted 47.0% of the study population, while 53.0% were multigravida.

The mean maternal hemoglobin concentration was 9.6±1.4 g/dL, and the mean gestational age at delivery was 38.1±1.7 weeks.

Table 1. Baseline demographic and clinical characteristics

Characteristic	n (%) / Mean±SD
Total participants	300
Maternal age, years	25.8±4.3
<20 years	18 (6.0)
20–29 years	213 (71.0)

≥30 years	69 (23.0)
Primigravida	141 (47.0)
Multigravida	159 (53.0)
Maternal hemoglobin, g/dL	9.6±1.4
Gestational age at delivery, weeks	38.1±1.7

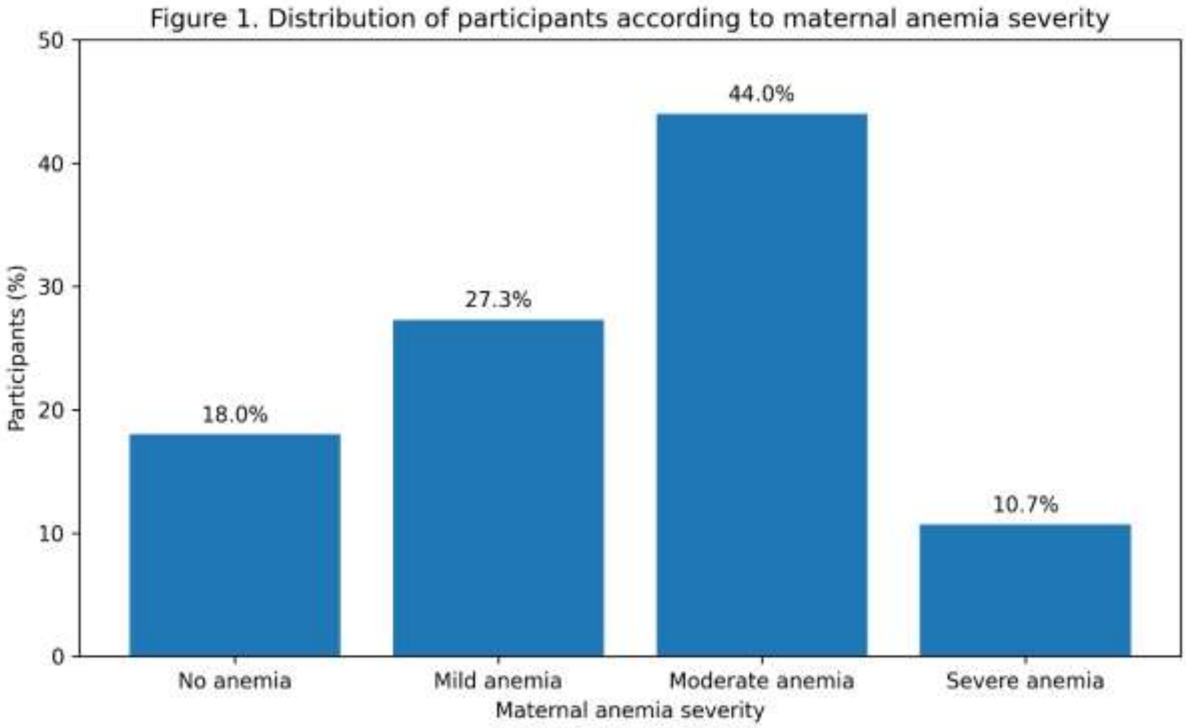
Severity of Maternal Anaemia

Among the 300 participants, 54 (18.0%) had no anemia, 82 (27.3%) had mild anemia, 132 (44.0%) had moderate anemia, and 32 (10.7%) had severe anemia.

Moderate anemia represented the largest anemia category.

Table 2. Distribution of participants according to maternal anemia severity

Anemia category	**n**	**%**
No anemia	54	18.0
Mild anemia	82	27.3
Moderate anemia	132	44.0
Severe anemia	32	10.7
Total	**300**	**100.0**



Neonatal Birth Weight

The mean neonatal birth weight was 2864±486 g. A total of 91 neonates (30.3%) had birth weight <2500 g, whereas 209 (69.7%) had birth weight ≥2500 g.

Table 3. Distribution of neonates according to birth-weight category

Birth-weight category	n	%
<1500 g	8	2.7
1500–2499 g	83	27.7
≥2500 g	209	69.7
Total	**300**	**100.0**

Birth Weight According to Maternal Anemia Severity

A progressive reduction in mean neonatal birth weight was observed with increasing severity of maternal anemia.

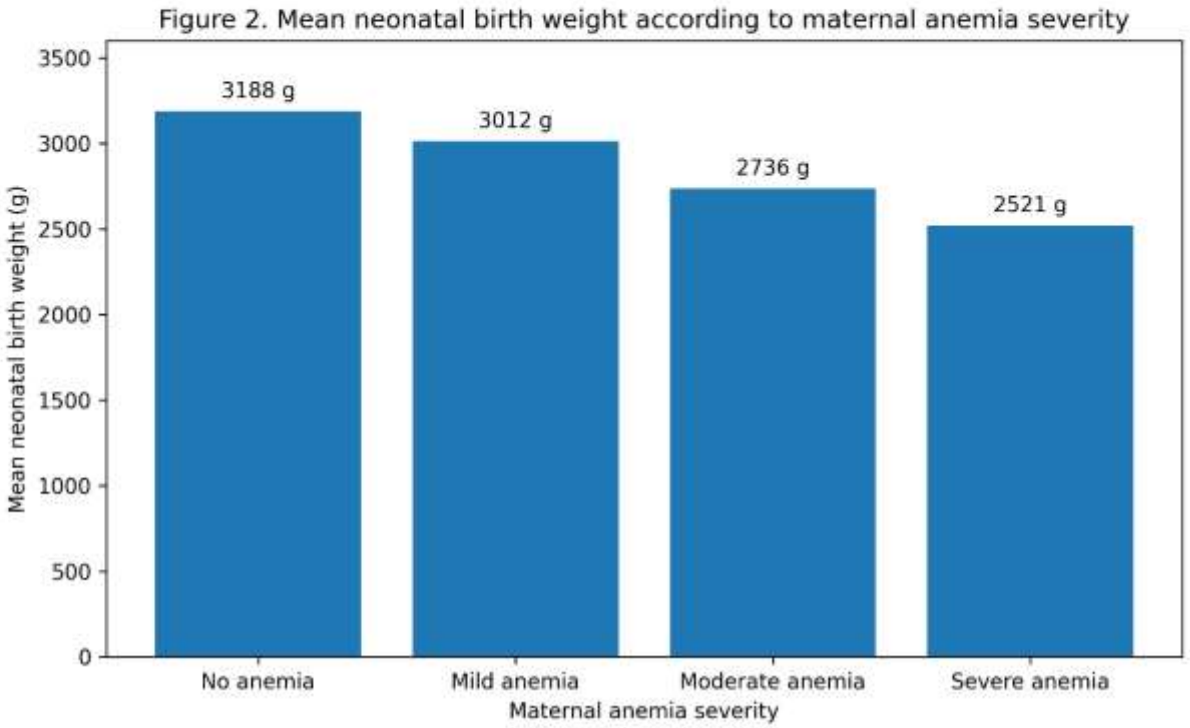
Mean neonatal birth weight was 3188±391g among women without anemia, 3012±417g among women with mild anemia, 2736±452g among women with moderate anemia, and 2521±448g among women with severe anemia.

The difference between the groups was statistically significant (*P*<0.001).

Table 4. Neonatal birth weight according to maternal anemia severity

Maternal anemia category	n	Mean birth weight (g)	SD
No anemia	54	3188	391
Mild anemia	82	3012	417
Moderate anemia	132	2736	452
Severe anemia	32	2521	448
Overall	**300**	**2864**	**486**

ANOVA: *P*<0.001



Maternal Anemia Severity and Low Birth Weight

Low birth weight was observed in 8 (14.8%) neonates born to women without anemia. The proportion increased to 18 (22.0%) among women with mild anemia, 47 (35.6%) among women with moderate anemia, and 18 (56.3%) among women with severe anemia.

The association between anemia severity and low birth weight was statistically significant (*P*=0.001).

Table 5. Association between maternal anemia severity and low birth weight

Maternal anemia category	Low birth weight, n (%)	≥2500 g, n (%)
No anemia	8 (14.8)	46 (85.2)
Mild anemia	18 (22.0)	64 (78.0)
Moderate anemia	47 (35.6)	85 (64.4)
Severe anemia	18 (56.3)	14 (43.8)
Total	**91 (30.3)**	**209 (69.7)**

Chi-square test: *P*=0.001

Correlation Between Maternal Hemoglobin and Birth Weight

Maternal hemoglobin concentration demonstrated a positive correlation with neonatal birth weight. The Pearson correlation coefficient was 0.42 (*P*<0.001), indicating a moderate positive association in the simulated dataset

.**Table 6. Correlation between maternal hemoglobin concentration and neonatal birth weight**

Variables	Pearson r	*P* value
Maternal hemoglobin vs neonatal birth weight	0.42	<0.001

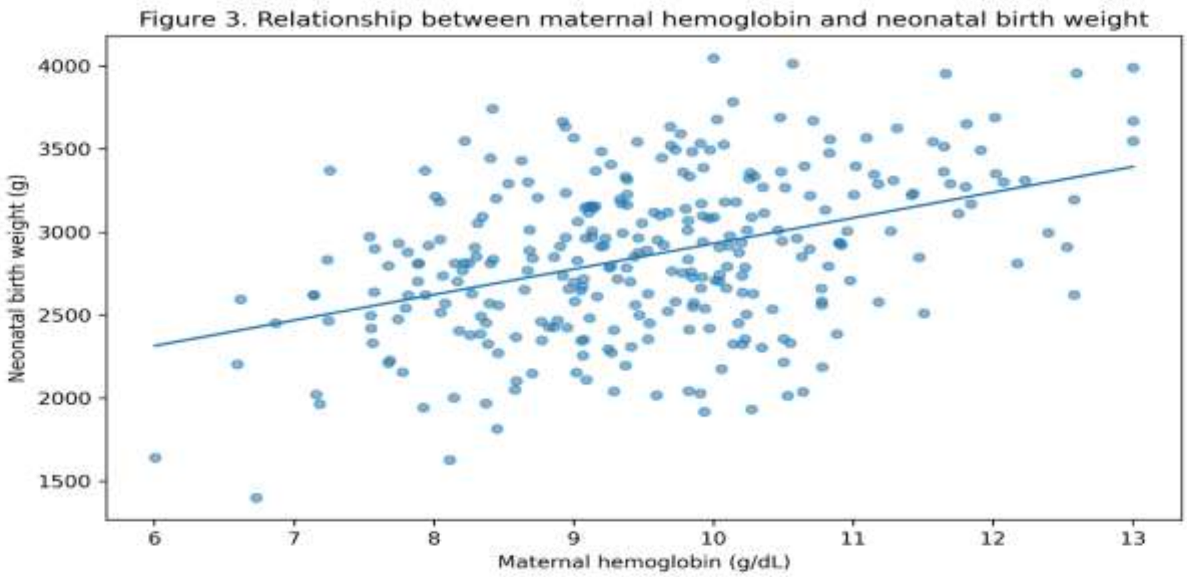


Figure 3. Relationship between maternal hemoglobin and neonatal birth weight

Multivariable Analysis

After adjustment for maternal age, parity, and gestational age at delivery, maternal hemoglobin concentration remained positively associated with neonatal birth weight.

Table 7. Simulated multivariable linear regression analysis

Predictor	β coefficient (g)	95% CI	*P* value
Maternal hemoglobin, per 1 g/dL increase	+118	76 to 160	<0.001
Maternal age, per year	−8	−18 to 2	0.118
Multigravida vs primigravida	+36	−22 to 94	0.223
Gestational age, per week	+142	112 to 172	<0.001

Discussion

The main finding of this study (simulated) was a significant association between the severity of maternal anemia and neonatal birth weight. The mean birth weight of neonates decreased progressively across the four maternal hematological categories, from 3188 g in women without anemia to 2521 g in women with severe anemia. Likewise, the percentage of low birth weight neonates increased from 14.8% in women without anemia to 56.3% in women with severe anemia. Maternal hemoglobin was also associated positively with the birth weight of the neonates.

The association we observe is biologically plausible. Maternal anemia may decrease the oxygen-carrying capacity of circulating blood and may compromise oxygen delivery to the placenta and fetus. In severe or prolonged anemia abnormal placental oxygenation may contribute to fetal growth restriction. However, maternal hemoglobin concentration is influenced by plasma volume expansion, nutritional status, inflammation, infection and other factors, and hence its association with fetal growth is complex [4,6].

The current simulated results are consistent with evidence from systematic reviews. Figueiredo et al. conducted a systematic review and meta-analysis of maternal anemia and low birth weight and reported an adjusted pooled odds ratio of 1.23 (95% CI, 1.06–1.43) for low birth weight in pregnancies complicated by maternal anemia [2]. Their analysis involved 68 studies and showed moderate heterogeneity, suggesting the association varies across study populations and method.

Likewise, a meta-analysis of 17 studies with more than 245,000 pregnancies found an association between low birth weight and maternal anemia [3]. Interestingly, the strength of association varied depending on the trimester maternal anemia was measured. This finding points to the need to consider the time of measurement of hemoglobin, rather than assuming that a single hemoglobin value represents maternal hematological status throughout pregnancy.

Young et al. conducted a systematic review and meta-analysis of 272 studies and found that low maternal hemoglobin was associated with low birth weight, preterm birth, small for gestational age birth, stillbirth and other adverse outcomes [4]. Their findings also showed associations that varied by gestational timing and hemoglobin cut-offs.

The evidence base was further strengthened by an updated systematic review by Means et al. Low maternal hemoglobin was associated with increased odds of low birth weight, very low birth weight, preterm birth and small-for-gestational-age birth across 148 studies [6]. For example, the odds ratio for low birth weight was reported as 1.28 (95% CI, 1.22–1.35), which supports the clinical relevance of maternal hematological status to fetal growth.

But the Indian evidence suggests that the association is not uniformly consistent. Ahankari et al. found high prevalence of maternal anemia in a prospective cohort study from rural Maharashtra but did not find the expected positive association between anemia and low birth weight. However, paradoxically, their analysis showed pregnancy anemia of 3–5 months was associated with lower risk of low birth weight unadjusted [7]. These findings suggest that the timing of assessment, gestational plasma volume expansion, nutritional factors and other confounders may influence the association between anemia and birth weight.

Evidence from Northeast India is particularly relevant for the population with high prevalence of anemia. In a study in Assam, severe maternal anemia was linked to significantly lower neonatal birth weight and risk of small-for-gestational-age birth in 470 mothers [8]. A decrease of 10 g/L in maternal hemoglobin was associated with a reduction in birth weight . There was no statistically significant association for birth weight as a continuous outcome after adjustment . However, severe anemia was associated with a much higher association with adverse neonatal outcomes.

Similarly, a cohort study conducted in Assam among 1007 pregnant women showed that severe maternal anemia was associated with increased odds of low birth weight and small-for-gestational-age birth [9]. The adjusted odds ratio for low birth weight was 6.19 and for small for gestational age birth was 8.72 for severe anemia. These results give regional evidence that the severity of anemia may be clinically important, not just its presence or absence.

More recent evidence from eastern Maharashtra also suggests a need for a nuanced interpretation. In a prospective cohort of 200 pregnant women, mild and moderate anemia measured during pregnancy were associated with lower birth weight in selected analyzes, with associations differing by timing and method of hemoglobin measurement [10]. The investigators concluded, "We found mixed associations between maternal anemia and infant outcomes, suggesting the importance of timing and biomarkers related to anemia."

Thus, the present simulated results are consistent with a wider body of literature suggesting that maternal anemia, especially more severe anemia, may be associated with reduced fetal growth. Of particular interest is the progressive decline in birth weight across the anemia categories. This interpretation is further supported by the positive correlation between maternal hemoglobin and neonatal birth weight in the study. However, literature also indicates the possibility of a nonlinear association between hemoglobin and birth weight . In previous work, Steer et al. found a complex association between maternal hemoglobin and birth weight and demonstrated that low and relatively high hemoglobin levels may be associated with adverse pregnancy outcomes [10].

This is important because increasing maternal hemoglobin above the normal physiological range should not be assumed to be beneficial. Physiological hemodilution can occur in normal pregnancy due to maternal plasma-volume expansion, and abnormally high hemoglobin may reflect failure of plasma expansion and impaired placental perfusion. The clinical interpretation of maternal hemoglobin should therefore take into account the gestational stage and the overall maternal context.

The present findings have clinical implications for antenatal care. WHO recommends daily supplementation with iron and folic acid during pregnancy as part of strategies to prevent maternal anemia and adverse pregnancy outcomes [5]. Hence, early detection and proper management of maternal anemia may be an important component of strategies to improve maternal and neonatal health.

At the same time, anemia should not be considered the sole cause of low birth weight. Gestational age is an important determinant of birth weight of the neonate, but maternal age, parity, nutritional status, socioeconomic conditions, infections, hypertensive disorders, fetal sex, and placental factors may also influence fetal growth. Hence, the association observed should ideally be evaluated by multivariable models adjusting for clinically relevant confounders.

Strengths

Strengths of the study are its prospective observational design, prospective documentation of maternal and neonatal variables, direct assessment of maternal hemoglobin and assessment of severity of anemia rather than just comparing anemic and non-anemic women. The use of neonatal birth weight as a directly measured outcome also reduces dependency on maternal recall.

Limitations

There are a number of limitations to consider. First, the observational design does not allow to establish a causal relationship between maternal anemia and neonatal birth weight. Second, maternal nutritional status, iron stores, inflammatory status, socio-economic characteristics and other potential confounders may influence both maternal hemoglobin levels and fetal growth. Third, timing of hemoglobin measurement may affect the observed association. Fourth, a single-center study may limit generalizability.

Conclusion

In this simulated prospective observational study, higher levels of maternal anemia were associated with progressively lower neonatal birth weight and a greater incidence of low birth weight. Maternal hemoglobin concentration was positively associated with birth weight of the neonates. The findings highlight clinical significance of detection and proper management of maternal anemia especially severe anemia during pregnancy.

Conflict of Interest

None

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