

A relação entre as concentrações de hemoglobina durante a gravidez e peso de nascimento

The relationship between hemoglobin concentrations during pregnancy and birth weight

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RESUMO

Objetivo: Avaliar a relação entre as concentrações de hemoglobina (Hb) durante a gravidez e o peso ao nascer. Métodos: Estudo transversal envolvendo 1450 gestantes e seus recém-nascidos atendidos em maternidade pública do Rio de Janeiro, Brasil (1999–2014). As concentrações de Hb foram avaliadas nos três trimestres da gestação e o peso ao nascer foi avaliado como variável contínua e como variável dicotômica: baixo peso ao nascer (<2.500,00 g) e peso normal (> 2.500,00 g). A relação entre Hb e peso ao nascer foi avaliada por meio de regressão linear múltipla. Curvas ROC foram utilizadas para identificar pontos de corte para Hb com melhor sensibilidade e especificidade para baixo peso ao nascer. Resultados: Nos modelos explicativos para o peso ao nascer, verificou-se que as concentrações de Hb foram negativamente associadas ao peso ao nascer nos três trimestres da gravidez (1º trimestre: $\beta = -45,02$, IC 95% - 75,18 a -14,86; 2º trimestre: $\beta = -45,02$, IC 95% -57,18 a -4,87; 3º trimestre: $\beta = -38,11$, IC 95% -60,77 a -15,46), controlando para idade gestacional no parto, ganho de peso gestacional, número de partos anteriores e pré- IMC gestacional. O peso médio ao nascer foi significativamente maior entre as mulheres nos quartis inferiores de Hb no primeiro ($p = 0,012$) e no terceiro ($p = 0,002$) trimestres. Os valores de Hb relacionados ao baixo peso ao nascer no 1º, 2º e 3º trimestres foram 12,6 g / dL, 11,4 g / dL e 12,35 g / dL, respectivamente. Conclusão: Os resultados sugerem uma associação inversa entre maiores concentrações de Hb e menor peso ao nascer.

Palavras-chaves: Hemoglobina, Gravidez, Recém-nascido, Peso ao nascer, Suplementos Alimentares.

ABSTRACT

Objective: To evaluate the relationship between hemoglobin (Hb) concentrations during pregnancy and birth weight. Methods: Cross-sectional study involving 1450 pregnant women and their newborns who attended a public maternity hospital in Rio de Janeiro, Brazil (1999–2014). Hb concentrations were assessed in the three trimesters of pregnancy and birth weight was assessed as a continuous variable and as a dichotomous variable: low birth weight (< 2500.00 g) and normal weight (> 2500.00 g). The relationship between Hb and birth weight was assessed using multiple linear regression. ROC curves

were used to identify cutoff points for Hb with better sensitivity and specificity for low birth weight. Results: In the explanatory models for birth weight, it was found that Hb concentrations were negatively associated with birth weight in all three trimesters of pregnancy (1st trimester: $\beta = -45.02$, 95% CI - 75.18 to -14.86; 2nd trimester: $\beta = -45.02$, 95% CI -57.18 to -4.87; 3rd trimester: $\beta = -38.11$, 95% CI -60.77 to -15.46), controlling for gestational age at delivery, gestational weight gain, number of previous deliveries, and pre-gestational BMI. Mean birth weight was significantly higher among the women in the lower Hb quartiles in the first ($p = 0.012$) and third ($p = 0.002$) trimesters. The Hb values related to low birth weight in the 1st, 2nd, and 3rd trimesters were 12.6 g/dL, 11.4 g/dL, and 12.35 g/dL, respectively. Conclusion: The results suggest an inverse association between higher Hb concentrations and lower birth weight.

Keywords: Hemoglobin, Pregnancy, Newborn, Birth weight, Dietary Supplements.

1 INTRODUCTION

Anemia is considered one of the main complications in pregnancy in developing countries and a serious public health problem worldwide (1,2). Data from the World Health Organization (WHO) reveal that anemia affects about 29% (496 million) non-pregnant women and 38% (32.4 million) pregnant women aged 15–49 years (3). Hemoglobin concentration (Hb) is often used to investigate and diagnose anemia, and its measurement is part of the prenatal care provided at public health facilities in Brazil because it is a simple, low-cost method (4).

However, studies have shown that variations in Hb concentrations are not always associated with nutritional deficiencies, and that high Hb concentrations may be a risk factor for the development of gestational diabetes mellitus and pre-eclampsia, as well as unfavorable outcomes that can affect the mother and child (5–8). It is suggested that there is a U-shaped curve for high and low maternal Hb concentrations and the risks of adverse maternal and perinatal outcomes (9,10).

Malhotra et al (11) carried out a study with 447 women in order to assess the results of pregnancy and birth according to different degrees of maternal anemia. The sample was divided into four groups: group I (Hb > 11 g/dL), group II (Hb 9–10.9 g/dL), group III (Hb 7–8.9g/dL), and group IV (Hb < 7 g/dL). The offspring of the women in group II had a lower prevalence of low birth weight (LBW) and intrauterine growth restriction, with lower induction and surgical delivery rates. A study by Sehgal et al (12) revealed that the risk for unfavorable outcomes at birth rose in proportion to the severity of the maternal anemia.

The relationship between maternal Hb concentrations and birth weight remains inconclusive. It is believed that maternal hemoconcentration, attributed to reduced plasma

volume expansion, may influence blood viscosity and, consequently, lower placental perfusion, restricted fetal growth and a higher risk of pregnancy complications (13). While iron deficiency anemia continues to be a significant problem around the world, it is worth reflecting on the Hb cutoff points for the diagnosis of anemia in pregnancy and reviewing the strategies for its treatment, including iron supplementation. This study aims to assess maternal hemoglobin concentrations and correlate them with the birth weight of the infants of women who attend a public maternity hospital in Rio de Janeiro.

2 MATERIALS AND METHODS

2.1 STUDY DESIGN

This cross-sectional study was undertaken by analyzing a research database developed under the responsibility of the Research Group on Maternal and Child Health of the Josué de Castro Institute of Nutrition (INJC) and the maternity teaching hospital of the Federal University of Rio de Janeiro (Maternidade Escola, UFRJ).

2.2 STUDY POPULATION

The original population consisted of 1450 adult women (chronological age > 20 years) with a singleton pregnancy and no chronic diseases who attended the prenatal care service of a public maternity hospital linked to the Brazilian public health system (SUS), in Rio de Janeiro, RJ, Brazil, between 1999 and 2014, and their respective newborns. The inclusion criteria for the selection of participants from the database were: availability of information on Hb concentrations in the first, second, and third trimesters of pregnancy and birth weight.

Because the number of women with available information for the present analysis was smaller than the total sample of the original study, post hoc calculations were performed. Assuming a 6% prevalence of LBW and a significance level of 5% and 80% power, the sample size of the current study (1387 women) was able to detect differences of at least 5% in the prevalence of LBW the groups.

2.3 ETHICS

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Ethics and Research Committee of Federal University of Rio de Janeiro Maternity School

(CAAE 64024217.5.00005275). Written informed consent was obtained from all subjects/patients.

2.4 DATA COLLECTION

For the diagnosis of gestational anemia, Hb concentration < 11 g/dL was used as the cutoff point in all trimesters of pregnancy (14,15). As for the degree of severity, anemia was classified into: mild to moderate (Hb > 8 and < 11 g/dL) and severe (Hb < 8 g/dL) (15).

Data were collected by a team of trained and supervised researchers by consulting the participants' medical records and via the face-to-face interviews with the nutritionist during prenatal care.

2.5 VARIABLES ANALYZED

The dependent variable was birth weight, assessed as a continuous variable (g) and stratified in LBW (< 2500 g), normal weight (≥ 2500 g), and macrosomia (≥ 4000 g) (16). The concentrations of maternal Hb throughout pregnancy were assessed as continuous (g/dL) and categorical variables, with values stratified in quartiles.

The covariables analyzed as continuous variables were: gestational age at delivery (weeks); pre-gestational nutritional status (via pre-gestational BMI, kg/m²); total gestational weight gain (kg); number of previous deliveries; and number of prenatal consultations. The variables used to characterize the sample are described below:

- Sociodemographic: maternal age at birth (20–34 years or ≥ 35 years); skin color (white or non-white); education (high school graduate or non-graduate); partnership status (partnered or unpartnered); place of residence (South Zone of Rio or elsewhere); housing conditions (adequate [regular waste collection, sewage, and running water] or inadequate [absence of all these services]) (17);
- Clinical: Complications during pregnancy (hypertensive disorders of pregnancy/others or none) (15,18).
- Obstetric and prenatal care: number of pregnancies (1st pregnancy / 2nd or more pregnancy), number of prenatal consultations ($<$ or ≥ 6), use of nutritional supplements during pregnancy (iron sulfate and/or folic acid or none or others), cigarette and alcohol consumption during pregnancy (yes or no);
- Anthropometric: pre-gestational BMI (weight [kg] divided by height [m²]), classified according to Brazilian Ministry of Health recommendations (16) into low

weight (<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obesity (30 kg/m²). The adequacy of gestational weight gain was classified as recommended by the Institute of Medicine (19).

2.6 STATISCAL ANALYSIS

Measures of central tendency and dispersion (mean and standard deviation, SD) were calculated for the analysis of the continuous variables. Student's t-test was used to assess the difference between two means. The chi-squared test was used to analyze the categorical variables. The Hb concentrations per trimester were divided into quartiles. Significance was set at 5%.

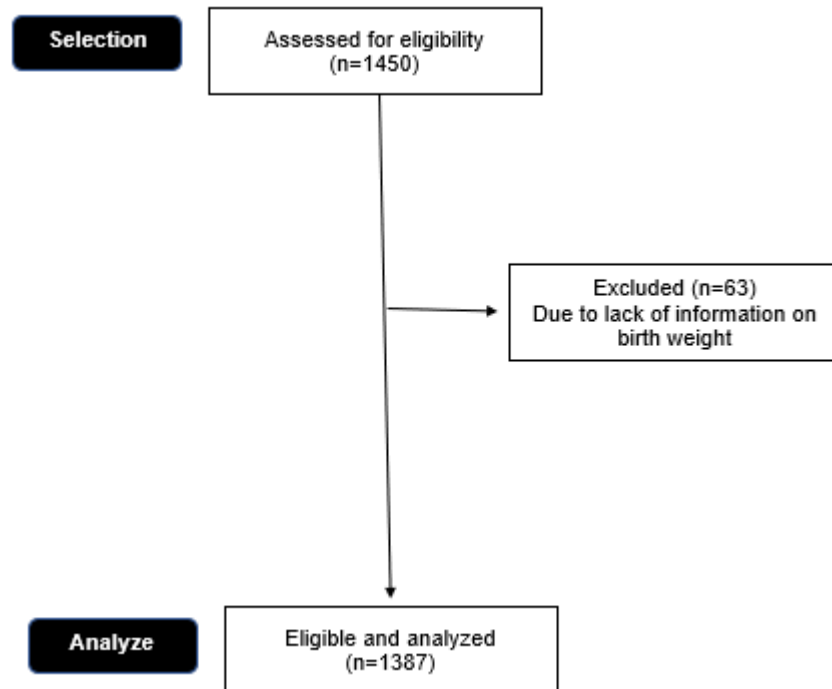
The bivariate linear regression was performed with weight at birth as the outcome and the following independent variables: gestational age at delivery (weeks); pre-gestational nutritional status; total gestational weight gain (kg); number of previous deliveries; and number of prenatal consultations. Next, multiple linear regression models were tested, including the variables with $p < 0.20$ in the bivariate analysis. The criterion for the inclusion of the variables in the final model was $p < 0.05$. The coefficients (gross β) were estimated and adjusted with their respective 95% confidence intervals (CI). All analyses were performed using SPSS Statistics for Windows, version 22.

Receiver operating characteristic (ROC) curves were plotted to identify cutoff points for the serum Hb values that offered the best combination of sensitivity and specificity for the corresponding LBW values of the newborns. MedCalc version 19.1 was used to prepare and analyze the data by means of the ROC curves. Significance for this analysis was set at 5%.

3 RESULTS

Data on 1450 women eligible for the study were retrieved, 63 (4.54%) of whom were excluded because birth weight data were missing (see Figure 1). The remaining 1387 women were 28.39 (+5.49) years old, 54.8% had graduated from high school, 73.9% were partnered, 46.2% had non-white skin color, 50.5% did not live in the South Zone of Rio de Janeiro, and 66.3% lived in housing with adequate sanitation. As for their prenatal care, 91.9% attended six or more prenatal consultations and 45.5% started prenatal care before 14 weeks. Cigarette use was reported by 6.4% of the participants and alcohol use was reported by 12.8%.

Figure 1 - Flowchart for obtaining the sample used in the study with information related to birth weight selection



Source: Prepared by the authors

As for obstetric history, 62.1% had had at least one prior pregnancy, 6.6% were diagnosed with gestational hypertensive disorders, and 28.3% were diagnosed with iron deficiency anemia, whose prevalence was higher in the second trimester of pregnancy (18.8%) than in the first (3.2%) or the third (16.1%). In all three trimesters, mild anemia (Hb 10–10.99 g/dL) was more prevalent than moderate or severe anemia (1st trimester 2.5%, 2nd trimester 15.6%, 3rd trimester 13.7%). The use of supplements with ferrous sulfate and/or folic acid during pregnancy was reported by 69.9% of the participants.

The pre-gestational BMI data revealed that 57.9% of the participants were normal weight, while 15.6% had total gestational weight gain below the recommended level. Mean gestational age at birth was 39.03 weeks (SD = 1.87) and mean birth weight was 3275.18 g (SD = 517.80), with 5.0% (n = 69) LBW, 89.7% (n = 1244) adequate weight, and 5.3% (n = 74) macrosomia.

Table 1 describes the independent variables related to birth weight in simple linear regression ($p < 0.20$): Hb in the 1st trimester ($p = 0.027$), 2nd trimester ($p = 0.081$), and 3rd trimester ($p = 0.002$); pre-gestational BMI ($p = 0.000$); total gestational weight gain ($p = 0.000$); maternal age ($p = 0.103$); gestational age at delivery ($p = 0.000$); number of

previous deliveries ($p = 0.001$); household size ($p = 0.011$); number of prenatal consultations ($p = 0.000$).

Table 1: Model using simple linear regression obtained from the relationship between maternal hemoglobin concentration, anthropometric, obstetric, and sociodemographic characteristics, prenatal care, and birth weight among women who attended Maternidade Escola, UFRJ (Rio de Janeiro, RJ, Brazil, 1999–2014).

Variables	Gross β	p	CI (95%)
<i>Clinical Variable (hemoglobin)</i>			
Hb 1st trimester (g/dL)	-43.72	0.027	-82.43, -5.00
Hb 2nd trimester (g/dL)	-29.69	0.081	-63.00, -3.62
Hb 3rd trimester (g/dL)	-40.27	0.002	-66.30, -14.25
<i>Anthropometric Variables</i>			
Nutritional status (pre-gestational BMI – kg/m ²)	12.06	0.000	5.66, 18.46
Total gestational weight gain (kg)	22.23	0.000	17.34, 27.11
<i>Obstetric and sociodemographic variables</i>			
Maternal age (years)	-4.13	0.103	-9.11, 0.84
Gestational age at delivery (weeks)	157.26	0.000	145.31, 169.22
Number of previous deliveries	51.46	0.001	21.72, 81.20
Household size	31.12	0.011	7.253, 54.98
<i>Prenatal variables</i>			
Number of prenatal consultations	52.34	0.000	41.34, 63.34

Legend: Hb - hemoglobin; 95% CI - 95% confidence interval; β - Coefficient of linear regression; p - p-value.

Source: Prepared by the authors

Table 2 presents three explanatory models for birth weight obtained in the bivariate linear regression, considering the Hb concentrations throughout pregnancy. Controlling for gestational age at birth (weeks), which is the variable that has the greatest impact on birth weight, as described in models I, II and III, it was found that a one-unit increase in Hb concentration during pregnancy contributed to the following reductions in birth weight: -43.72g (95% CI -82.43 to -5.00) in the 1st trimester (model I); -29.69g (95% CI -63.00 to -3.62) in the 2nd trimester (model II); and -40.27g (95% CI -66.30 to -14.25) in the 3rd trimester (model III), controlling for the effect of pre-gestational BMI, total gestational weight gain, number of prenatal consultations, in addition to gestational age at delivery.

In the multiple linear regression models (Table 2), a negative association between Hb concentrations and birth weight in all three trimesters of pregnancy was confirmed (1st trimester: adjusted $\beta = -45.02$, 95% CI -75.18 to -14.86 ; 2nd trimester: adjusted $\beta = -45.02$, 95% CI -57.18 to -4.87 ; 3rd trimester: adjusted $\beta = -38.11$, 95% CI -60.77 to -15.46).

Table 2: Multiple linear regression of the predictive factors of birth weight, Maternidade Escola, UFRJ (Rio de Janeiro, RJ, Brazil, 1999–2014)

Models	Gross β	CI (95%)	Adjusted β	CI (95%)
<i>Model I – R² 0.437</i>				
Gestational age at delivery (weeks)	157.26	145.31 – 169.22	153.12	136.49, 169.75
Prenatal nutritional status (pre-gestational BMI (kg/m ²))	12.06	5.66 – 18.46	21.894	14.45, –29.34
Total gestational weight gain (kg)	22.23	17.34 – 27.11	21.910	16.06, 27.76
Number of previous deliveries	51.46	21.72 – 81.20	45.49	10.57, 80.40
Number of prenatal consultations	52.34	41.34 – 63.34	10.68	–4.52, 25.88
Hb in 1st trimester (g/dL)	–43.72	–82.43 – –5.00	–45.02	–75.18, –14.86
<i>Model II – R² 0.426</i>				
Gestational age at delivery (weeks)	157.26	145.31 – 169.22	151.50	137.41, 165.59
Prenatal nutritional status (pre-gestational BMI)	12.06	5.66 – 18.46	15.05	8.65, 21.46
Total gestational weight gain (kg)	22.23	17.34 – 27.11	17.66	12.64, 22.68
Number of previous deliveries	51.46	21.72 – 81.20	54.81	25.81, 83.83
Number of prenatal consultations	52.34	41.34 – 63.34	7.52	–5.39, 20.44
Hb in 2nd trimester (g/dL)	–29.69	–63.00 – –3.62	–45.02	–57.81, –4.87
<i>Model III – R² 0.286</i>				
Gestational age at delivery (weeks)	157.26	145.31 – 169.22	150.62	132.16, 169.08
Prenatal nutritional status (pre-gestational BMI)	12.06	5.66 – 18.46	16.01	9.61, 22.40
Total gestational weight gain (kg)	22.23	17.34 – 27.11	17.46	12.41, 22.50
Number of previous deliveries	51.46	21.72 – 81.20	48.85	20.08, 77.63
Number of prenatal consultations	52.34	41.34 – 63.34	–0.243	–12.79, 12.30
Hb in 3rd trimester (g/dL)	–40.27	–66.30 – –14.25	–38.11	–60.77, –15.46

Legend: 95% CI – 95% confidence interval; β – Coefficient of linear regression; p – p-value.
Source: Prepared by the authors

When comparing the average birth weights according to the quartiles of Hb concentration per trimester of pregnancy, higher average birth weights were found for the lowest Hb quartiles in the 1st ($p = 0.012$) and 3rd trimester ($p = 0.002$, Table 3).

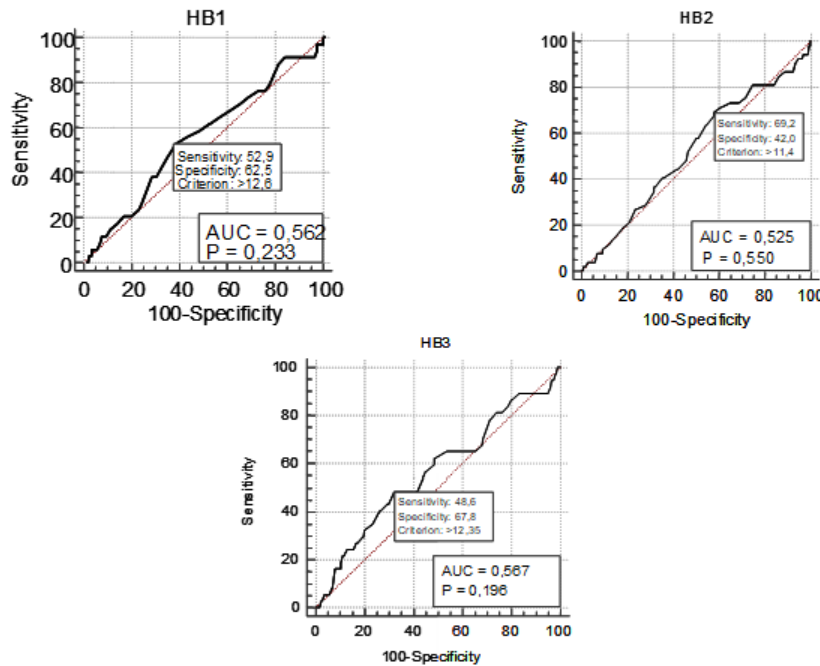
Table 3: Comparison of mean birth weight (g) according to quartiles of hemoglobin concentrations (Hb) by gestational trimester. Maternidade Escola, UFRJ (Rio de Janeiro, RJ, Brazil, 1999–2014)

Quartiles of Hb concentration per trimester	n	Mean birth weight (grams)	Standard deviation	p ^a
First Trimester				
Up to 12.4 g/dL ^b	381	3323.38	500.38	0.012
Above 12.4 g/dL ^c	351	3225.75	546.56	
Total	732	3276.56	524.94	
Second Trimester				
Up to 11.7 g/dL ^b	556	3298.08	494.20	0.084
Above 11.7 g/dL ^c	482	3242.03	549.14	
Total	1038	3272.05	520.94	
Third Trimester				
Up to 11.8 g/dL ^b	516	3351.08	442.92	0.002
Above 11.8 g/dL ^c	504	3258.75	496.70	
Total	1020	3305.46	472.30	

Legend: ^a Student's t-test; ^b first and second quartiles; ^c third and fourth quartiles.
Source: Prepared by the authors

From the analysis of the ROC curves, it can be seen that the correlations between maternal Hb and LBW were positive and significant per trimester of pregnancy. The Hb cutoff point related to LBW was 12.6 g/dL in the 1st trimester, 11.4 g/dL in the 2nd trimester, and 12.35 g/dL in the 3rd trimester (Figure 2).

Figure 2: The ROC curve (area) of the hemoglobin rates of the mothers and heavy birth of your child in first (HB1), second (HB2) and third semester (HB3).



Source: Prepared by the authors

4 DISCUSSION

In this study, maternal Hb concentrations throughout pregnancy showed a negative association with birth weight after controlling for the effect of the modifiable variables gestational age at delivery and total gestational weight gain, and the non-modifiable variables pre-gestational BMI and number of previous deliveries. These findings suggest that changes in maternal Hb concentrations during pregnancy were inversely associated with birth weight. These results corroborate previous studies (11, 20, 21).

One possible explanation for the findings is the change in the hematological profile associated with the physiological adaptation of pregnancy, which affects Hb concentration and plasma volume expansion, leading to maternal hemodilution, facilitating placental perfusion (22–24). This hemodilution and the associated reduction in blood viscosity has been considered a positive factor for the transport of oxygen and nutrients to the fetus, favoring birth weight (13, 23, 24).

Anemia was diagnosed in 28.3% of the women studied, with a higher percentage in the second trimester of pregnancy (18.8%). This result could be explained by the physiological changes in maternal Hb concentration, which decreases from the second

trimester of pregnancy until around the 24th week. As such, this result cannot be interpreted as a pathological finding without full prior knowledge of such changes (25, 26).

In our study, the lowest quartiles of Hb concentration during pregnancy were positively associated with birth weight, with the greatest impact in the first and second trimester. The study by Jwa et al. (20) showed similar results in adult pregnant women with a mean age of 35.5 years. They found that a +1 g/dL increase in Hb concentration from the beginning to the end of the pregnancy was associated with a -76.1 g change in birth weight and that the highest Hb concentrations were associated with the highest risk of LBW.

Another possible explanation for the association between higher mean birth weight and lower maternal Hb is the relationship between maternal hematological values and the expression of Flt-1 and Flk-1 receptors, responsible for vascular endothelial growth factor and placental growth factor, as suggested by Stangret et al. (22). It has been observed that Hb concentrations between 9.7 g/dL and 10.8 g/dL can result in decreased oxygen capacity in the blood, leading to hypoxemia. Reduced Hb concentration is essential for the positive regulation of these receptors in the formation of new blood vessels (angiogenesis) and increased fetal placental vascularization, improving the transfer of nutrients between mother and fetus (22).

In a systematic review and meta-analysis, Jung et al. (27) found that the risk for adverse outcomes in pregnancy is increased when the Hb concentration reaches levels outside the normal range for this phase.

In the present study, the following cutoff points for maternal Hb were set in relation to the occurrence of LBW: 12.6 g/dL (1st trimester), 11.4 g/dL (2nd trimester), and 12.35 g/dL (3rd trimester). Milasinović et al. (28) found that pregnant women with Hb values > 11.7 g/dL and ferritin concentrations above 13.6 ng/mL and hematocrit > 32.9% in the 30th to 32nd week of pregnancy were more likely to have restricted intrauterine growth and LBW infants, according to the analysis of the ROC curve. Their proposed cut-off point for Hb was similar to that found in the second trimester of pregnancy (11.4 g/dL) in our study.

Iron deficiency can be identified at an early stage by assessing serum ferritin. Serum concentrations below 15 µg/dL in the first trimester of pregnancy indicate depletion of cellular iron stores, motivated by insufficient consumption, absorptive inefficiency, and/or increased losses (parasitic infections, hemorrhages) (29). In advanced

stages, the production of red blood cells is compromised, and anemia can be detected by hemoglobin concentrations (≤ 11 g/dL in the first and third quarters and ≤ 10.5 g/dL in the second quarter) (30). In 2020, the WHO began to recommend the assessment of serum or plasma ferritin to identify iron status, as this parameter correlates with total body iron stores and serves to identify iron deficiency and iron overload in the body. Ferritin can be assessed together with hemoglobin to identify anemia (29).

Physiological changes in pregnancy, such as blood volume expansion, blood composition, and inflammatory status, may hamper any effort to define a single cut-off point for the diagnosis of iron deficiency during pregnancy based solely on ferritin concentration. Inflammation, C-reactive protein (CRP), α -1 acid glycoprotein (AGP), and additional iron indices, such as the soluble transferrin receptor, must be analyzed together (29).

It is recognized that LBW has a multicausal etiology, with prematurity being an important cause, as it is known that the shorter the duration of pregnancy, the smaller the size and weight of the newborn and the greater the risk of disability, mortality, and morbidity (31, 32). Capelli et al. (33) found that maternal anthropometric variables such as weight and pre-gestational BMI are positively associated with birth weight, reinforcing the importance of adequate pre-gestational nutritional status in order to improve conditions at birth, minimizing the risk of high or low birth weight. In the present study, the relationship between Hb concentrations and birth weight was demonstrated, controlling for the effect of gestational weight gain. Petry et al. (34) observed that age is one of the risk factors for anemia in children. In the study it was found that the prevalence of anemia was about twice as high in younger children (6 to 35 months) than older children (36 to 59 months, $p < 0.005$).

One of the main anemia prophylaxis strategies in Brazil is iron supplementation for all pregnant women, regardless of their iron status (35). However, the findings in the literature on the effect of iron supplementation during pregnancy are contradictory, as a series of reports have suggested negative impact associated with indiscriminate iron supplementation during pregnancy. A greater risk of thrombosis is highlighted by the elevation of placenta aggregation, pregnancy-induced hypertension, restricted intrauterine growth, and elevated oxidative stress, promoting increased free radicals leading to cell membrane damage, especially when associated with other nutrients such as vitamin C (36, 24).

Other findings suggest that iron supplementation may reduce the absorption of essential minerals during pregnancy, such as zinc (37), and other studies warn that iron supplementation among non-anemic pregnant women may negatively affect perinatal outcomes (38, 39). On the other hand, the use of ferrous sulfate supplement in women with pre-gestational anemia has been found to have a positive effect on birth weight (40). Iron supplementation in pregnant women without a diagnosis of anemia should be carefully evaluated, especially when the hematological profile is unaltered (41). According to Milman (42), from a nutritional point of view, iron prophylaxis during pregnancy should be prescribed on a case-by-case basis according to maternal stores.

The Ministry of Health guidelines for iron and folic acid supplementation in Brazil (15, 35) recommend a daily dose of 200 mg ferrous sulfate, which corresponds to 40 mg elemental iron. However, they contain discrepancies regarding the start of supplementation and the dosage of folic acid to be administered. One of the best known strategies in Brazil is routine supplementation with folic acid and ferrous sulfate for all pregnant women, regardless of screening for anemia, combined with the use of 400 µg folic acid until the end of pregnancy (35). Another recommended strategy is iron supplementation for women with Hb < 11 g/dL or chronic diseases, even without having anemia, and the use of 5 mg folic acid up to 3 months before conception and during the first trimester of pregnancy (15).

A study by Viteri et al. (38) sought to determine, in non-anemic pregnant women (Hb > 11.5 g/dL), whether oxidative stress was produced by the weekly or daily preventive supplementation of iron combined with other nutrients such as folic acid and vitamin B12. They found that after 8 weeks of daily supplementation, the Hb concentrations of 19.5% of the women rose to 14.5 g/dL. The group that received weekly supplementation had a lower incidence of increased Hb in pregnancy. This finding shows how harmful iron supplementation can be, because, as already demonstrated in other studies, high Hb values during pregnancy can trigger adverse effects (5–8).

The limitations of the present study include the low prevalence of pregnant women with very low (severe) Hb concentrations, making it difficult to identify significant differences in birth weight under this condition. In addition, our study population included relatively limited data on Hb concentrations in the first trimester.

5 CONCLUSION

Although maternal anemia is a major public health problem in Brazil and other developing countries, which can result in adverse perinatal consequences for the mother and child, attention should be paid to universal ferrous sulfate supplementation for pregnant women with and without anemia, as recommended by national and international health committees, given the possible negative influence of higher concentrations of maternal Hb (which can be associated with iron supplementation) on birth weight. The findings of the present study indicate an inverse association between maternal Hb concentrations and birth weight. Although the mechanisms that explain this finding have not yet been fully elucidated, it is extremely important for new studies to be undertaken that address the theme and for existing supplementation regimens to be reviewed, especially in terms of their applicability to pregnant women without anemia. Additionally, cutoff points for Hb should be set per trimester of pregnancy to assist the individualized prescription of iron supplementation for pregnant women.

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