Relationship between maternal hemoglobin and birthweight in Antioquia, Colombia

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Abstract

Objectives: to determine the relationship between maternal hemoglobin (HbM) per gestational trimester and birthweight (BW).

Methods: this was an analytical, cross-sectional observational study that included the prenatal records of 494 pregnant women who delivered live newborns in the Department of Antioquia. The maternal health data collected included HbM and BW, and gynecological and obstetric, anthropometric, and maternal health-related data. The Mann–Whitney U test was applied, supplemented by effect size (ES) to compare the study groups.

Results: HbM in the third trimester was significantly associated with BW (p=0.029).It showed a significant effect size on BW as follows: first trimester: ES=0.44 (CI95%= 0.183–0.697); second trimester: ES=0.49 (CI95%= 0.187–0.79); and third trimester: ES=0.43 (CI95% = 0.202–0.658). Maternal anemia was 4.2%, 11.2%, and 21.4% in the first, second, and third trimester, respectively.

Conclusions: as it is an inexpensive indicator and easy to determine, the timely monitoring and assessment of HbM is required owing to its importance in maternal and neonatal health, quality of life, and human capital development.

Key words *Birth weight, Anemia, Maternal hemoglobin, Pregnancy, Prenatal*

Introduction

Anemia is a nutritional problem that mainly affects women who are of reproductive age, pregnant women, and children under the age of 5 years; approximately 50% of cases are associated with iron deficiency. According to the 2011 global report, 38.2% of pregnant women have anemia.[1] The National Survey of the Nutritional Situation of Colombia (ENSIN) 2015 found anemia to be prevalent in 26.2% pregnant women aged between 13 and 49 years in Colombia, and 59.2% of these cases were due to iron deficiency;[2] according to the Food Nutritional Profile of Antioquia 2019, 48.4% of pregnant women had anemia.[3] Low birthweight (LBW) is associated with highly preventable nutritional and maternal care factors.[4,5] In 2016, approximately 20 million infants with LBW were recorded globally from among the developing countries[6] and according to the Administrative Department of Statistics, Colombia had a LBW prevalence of 8.7%[7] in 2014 and 9.2%[8] was recorded in Antioquia.

Anemia and LBW are important public health concerns associated with multiple factors and other health and nutrition determinants in women during their reproductive cycle.[4] The study by Sukrat *et al.*[9] and a meta-analysis of Ahankari *et al.*[10] are among the global studies analyzing the relationship between hemoglobin (HbM) during gestation and birthweight (BW) that coincide in affirming that low concentrations of HbM may affect BW. Furthermore, the study by Ahankari *et al.*[10] also found an unfavorable effect between high concentrations of HbM and BW. In Colombia, some studies have found a relationship between these two variables of interest and the context of the populations where they were conducted,[11,12] but none were found to directly associate HbM concentration with BW. In Medellín-Antioquia, there is some research that has addressed this problem, demonstrating the importance of maternal nutritional well-being on BW along with associated sociodemographic and gestational factors.[13,14] However, there are no municipal studies, or any from the Department of Antioquia, on HbM and BW. Therefore, this study determined the relationship between HbM concentration during gestation and the BW of live newborns (LNB), in the Department of Antioquia (Colombia).

Methods

This was an analytical, cross-sectional observational study of pregnant women who had LNB in the Department of Antioquia in 2014 (75,907 births).

The study sample consisted of prenatal medical records of 494 pregnant women obtained from municipal public health institutions of the nine subregions in the Department of Antioquia. Inclusion criteria were monofetal LNB from a pregnancy, data on the weight and length at birth of the newborn whose mother had a prenatal clinical record and at least one HbM reading at the institution of the birth of her child, mother's age at the time of birth between 15 and 40 years, healthy except for anemic conditions, and/or iron deficiency. Exclusion criteria were multiple pregnancies, obesity, underweight, and high obstetric risk.

The sociodemographic variables were taken from the file recommended by the Latin American Center for Perinatology, Sexual and Reproductive Health of Women (CLAP) as follows: age, educational level classified as primary (from 1 to 5 years of study), secondary (from 6 to 11 years of study), and university (pre- and post-graduate, more than 12 years of study), marital status, area of residence (urban or rural), ethnic group, health regime (contributory, uninsured, or subsidized), and their classification in the System of Identification of Social Program Beneficiaries (SISBEN). This regime places citizens in levels from zero to five, depending on their social and economic conditions, with level zero being the most deprived and vulnerable up to level five, who have the best conditions. Other variables were gynecological and obstetric: type of delivery, number of prenatal consultations, parity, weight of the last child, birth interval as reported in the CLAP file, referring to the time that has elapsed between the birth date of the last child and the beginning of the next pregnancy, planned or desired pregnancy; and anthropometric: pre-pregnancy or first trimester weight and height (body height), to eva-luate body mass index (BMI), as inclusion criterion.In cases where these data were not available, BMI was selected before week 20 to rule out pregnant women with obesity or those underweight in accordance with the Comprehensive Care Guidelines from the Ministry of Health and Social Protection of Colombia.[15]

HbM concentrations were taken from the clinical laboratory results of each health institution using the modified cyanmethemoglobin method[16] and later corrected according to altitude; the gestational age corresponding to each HbM was established by echography and these data defined the gestational trimester that corresponded to the HbM reading. Data obtained from the LNB included gestational age at birth, type of delivery, gender, BW, length, and head circumference. Weight was evaluated as a

continuous variable, as a ratio, to establish its correlation with HbM concentration and the BW categories were: for those born at full term, the World Health Organization (WHO)[4] classification system was used and the macrosomic cut-off according to Tamez-Perez et al.[17] (very LBW less than 1,499g, LBW less than 2500g, insufficient BW 2,500–2,999g; normal weight 3,000–4,000g, and macrosomic more than 4,000g); and for preterm patients, Fenton et al.[18] was used. The data collection was conducted using a previously adjusted and tested form designed by the group of researchers. Trained dietitian nutritionists made up the fieldwork staff.

For the description of the social demographic, gynecological and obstetric, and anthropometric aspects of the mother and the neonate, absolute and relative distributions were used with their 95% confidence intervals (CI95%) and summary indicators such as arithmetic mean, standard deviation, quartiles, and interquartile range. The Kolmogorov–Smirnov test was applied to assess the normality of the data. To calculate the delta (result of a mathematical operation, in this case, the difference in values) between the HbM of the first and third trimesters, the Wilcoxon signed-rank test was used. The relationship between HbM per gestation trimester and BW was determined using Spearman's correlation coefficient and the HbM per trimester was compared with the LNB weight categories (less than 3,000g and 3,000–4,000g) using the Mann–Whitney U test, supplemented with ES by means of probability of superiority (PS), where the following refe-rence values were taken: small ES between 0.1 and 2.9, medium between 0.3 and 0.49, and large ≥0.5[19] and the Eta coefficient squared, for the multivariate regression model. Multivariate regression was applied as an exploratory method by means of a generalized linear model of Poisson regression, with robust variance to adjust the proportion ratio (PR) and its CI95%, by multiple variables, in order to evaluate the effect of some maternal gynecological and obstetric characteristics in the classification of BW. For this, two categories of BW were outlined, based on biological plausibility, as follows: less than 3,000g and between 3,000g and 4,000g; the first included insufficient weight and underweight and the second included newborns of normal weight according to the WHO criteria, as mentioned in the LBW protocol.[4] A p value <0.05 was considered to be statistically significant. The data were processed using the SPSS version 23 program and the R Studio program, version 3.5.0.

The research was endorsed by the Bioethics Committee for Research in Humans at the University Research Headquarters (SIU- Universidad de Antioquia Nº. 17-69-761) and was carried out within the framework of resolution 8430 of 1993-Ministry of Health, the Declaration of Helsinki, and Resolution 839 of 2017-Ministry of Health and Social Protection of Colombia.

Results

The social demographic, gynecological and obstetric, and anthropometric characteristics of the pregnant women are described in Table 1. Regarding the level of education, the highest proportion of mothers had a high school-level (71.1%) education and 7.7% had no education; the majority resided in the urban areas of the Department of Antioquia (84%). The proportion of pregnant women who were single was 36.0%;furthermore, 77.3% belonged to level 1 of the SISBEN who were allowed by the national government to access social and health programs for people with very low social and economic resources. Gynecological and obstetric results revealed that only 27.1% of women had planned the pregnancy and 17.4% had had a previous abortion; only 20% of mothers had intergametic interval data in their prenatal record. Regarding the anthropometric data, median weight and pre-pregnancy BMI were 58 kg (53; 63) and 23.2 kg/m^{2} (21.7; 24.9), respectively; median body height was 157cm (153; 162).

Regarding HbM, 63% of measurements (n= 312) were obtained in the first trimester, with median 12.8g/dL and interquartile range 1.4 g/dL; 13 mothers (4.2%) had anemia, 3and 4 of whose condition continued in the second and third trimester, respectively. In the second trimester, 41.5% HbM results were obtained (n = 205), with median 11.9g/dL and interquartile range 1.5g/dL; 23 mothers (11.2%) had anemia and 8 of these continued to have the diagnosis at the end of pregnancy. In the third trimester, 74.3% HbM results were obtained (n=378), with median 11.9 g/dL and interquartile range 1.5 g/dL; 81 cases of anemia (21.4%) were evidenced, 8 of which were prevalent and 73 were new.

The anthropometric data and the nutritional classification of LNB are shown in Table 2. Mean BW was 3,225.5g ± 409.2. LBW and macrosomia were presented in the same proportion (3%) for each category (n = 15), and 23.5% of neonates (n = 116) were classified as having insufficient weight (Weight) (2,500–2,999g). Preterm LNBs were classified as follows: 83.3% (n = 15) adequate weight, 16.7%

(n=3) large for gestational age; none had the condition of small for gestational age.

When evaluating the relationship between HbM by trimester of gestation and BW, a linear correlation was not found. However, a statistically significant difference was found between the HbM in the third trimester and BW (*p*<0.029) when this variable was grouped into two categories according to biological plausibility (BW less than 3,000g and BW between 3,000g and 4,000g). Furthermore, when evaluating the effect size (ES), this was medium and important (ES more than 0.4) for HbM in each trimester (ES = 0.44, 0.49, and 0.43 in the first, second, and third trimester, respectively) and for the difference (delta) between HbM in the first and third trimesters (ES = 0.50) (Table 3).

In order to evaluate the relationship between the HbM, BMI, and several maternal gynecological and obstetric characteristics with BW according to the categories (BW less than 3000g and BW between 3000g and 4000g), a generalized linear Poisson regression model of robust variance was constructed. The candidate variables were chosen according to the criteria of statistical significance in the bivariate analysis and biological plausibility. Statistically significant differences were found between pre-pregnancy BMI and treated urinary tract infection (UTI) and BW (Table 4).

The decision of the significant variables was made by the adjusted PR in the multivariate model. Therefore, it is 2.53 times more likely for pregnant women with a UTI, even treated, to have a newborn weighing less than 3,000g compared with pregnant women without a UTI, adjusted for the other variables (PR = 2.53; CI95% = 1.24–5.18). In addition, the probability that a newborn has a weight less than 3,000g changes by a factor of 0.90 for each increase of one unit in pre-pregnancy BMI, adjusted for the other variables (PR = 0.90; CI95% = 0.81–0.99).

Discussion

There was a statistically significant association between the HbM in the third trimester and BW by category, and a medium and significant ES of the HbM was evidenced in each trimester, on the weight of the LNB. The results between the HbM and BW are heterogeneous,[20-24] which can be attributed to the treatment of the HbM variable in analysis because some researchers do not classify it by trimester of gestation and others assess it to define mothers with and without anemia, comparing its effect on BW, but without performing correlation analysis. Furthermore, the cut-off points for this diagnosis vary.

A review by Dewey *et al.*[22] concluded that a low HbM at the beginning of pregnancy is associated with LBW and adverse outcomes such as preterm, small for gestational age, and stillbirth, with the relationship being weak or non-existent with the second and third trimester HbM. Bakacak *et al.*[20] stated that the first trimester HbM was significantly associated with the BW being notably lower in the mothers of neonates with LW. However, second and third trimester HbMs were not associated with BW. By contrast, the meta-analysis by Ahankari *et al.*[10] showed that there was a greater effect of anemia on LBW in the first trimester compared with that in the second and third trimesters, and although this result was based on a small number of studies, it was corroborated by another meta-analysis by Figueiredo *et al.*[25] that also analyzed HbM in the first trimester and the adverse outcomes, with a significantly higher study size. This investigation also found a medium and important ES value of the first trimester HbM on the BW, as well as an effect of the second and third trimester HbMs on this LNB variable.

Urdaneta *et al.*[23] found a directly proportional and significant correlation between HbM and BW concentration (r = 0.439; *p* <0.0001), thus confirming the importance of this maternal protein in pregnancy outcomes. However, another investigation that analyzed the relationship between HbM and maternal serum iron levels in the third trimester, with BW and other pregnancy outcomes,[26] found no correlation or association between them.

In a study where there was a significant correlation between HbM and BW, in the group of mothers with anemia, it was observed that the gestation trimester was taken into account for the analysis, however, the maternal nutritional status, as an intervening variable, was not included.[27] Sacramento *et al.*[24] found no correlation between HbM during pregnancy and BW, except in the third trimester and among mothers with anemia. A similar result was evidenced in the meta-analysis of five studies conducted by Ahankari *et al.*[10] which showed that the LNB of women with anemia were, on average, 303g underweight compared with those who were born to mothers without anemia.

Regarding the difference or the HbM delta between the first and third trimesters, few studies evaluate the effect of this change on BW; to this regard, the study by Bakacak *et al.*[20] estimated the effect of the difference between HbM in the first and third trimesters (delta) on the BW categories and showed an LBW trend, wherein mothers had a lower change and with less variation, with respect to the

Table 1

Sociodemographic, gynecological and obstetric, and anthropometric characteristics of the pregnant women. Antioquia-Colombia.

Pregnant woman	N=494	Frequency % (CI95%)
Age in years		Me: 22 (19; 27)[a]
Educational level (years of study)		
None	38	7.7% (5.5–10.1)
From 1 to 5	71	14.4% (11.3–17.8)
From 6 to 11	351	71.1% (66.6–74.9)
More than 12	34	6.9% (4.9–9.3)
Residence area		
Urban	415	84.0% (80.8–87.0)
Rural	79	16.0% (13.0–19.2)
Ethnicity		
Mixed race	256	51.8% (47.2–56.3)
Black	19	3.8% (2.2–5.7)
Indigenous	4	0.8% (0.2–1.8)
Other	215	43.5% (39.3–48.2)
Marital status		
Common law marriage	266	53.8% (49.4 -58.1)
Single	178	36.0% (31.6–40.5)
Married	43	8.7% (6.3–11.3)
Other	7	1.4% (0.4–2.6)
Health regime		
Subsidized	426	86.2% (83.0–89.3)
Uninsured	55	11.1% (8.3–14.0)
Contributive	13	2.6% (1.4–4.0)
SISBEN[b] level		
Level 0	8	1.6% (0.6–2.8)
Level 1	382	77.3% (73.7–81.4)
Level 2	78	15.8% (12.6–19.2)
Level 3	25	5.1% (3.2–7.1)
Level 4	1	0.2% (0.0–0.6)
Gynecology and obstetrics		
Previous pregnancies	273	55.3% (50.8–59.5)
Previous abortions	86	17.4% (14.4–20.6)
Previous deliveries	231	46.8% (42.1–51.2)
Planned pregnancy	134	27.1% (23.1–31.2)
Birth interval	101	20.4% (16.8–23.9)
Cesarean	145	29.4% (25.3–33.4)
Treated UTI[c]	21	4.3% (2.4–6.1)
Anthropometrics		
Pregestational BMI[d]	494	Me: 23.2 (21.7; 24.9)[a]
Pregestational height (cm)	494	Me: 157 (153; 162)[a]
Pregestational weight (kg)	494	Me: 58 (53; 63)[a]
BMI[d] at last prenatal examination	494	Me: 27.2 (25.8; 29.0)[a]

[a] Data are shown in Me: median (lower quartile; upper quartile); [b] Health beneficiary identification system; [c] Urinary tract infection; [d] Body mass index.

Table 2

Anthropometric data and nutritional classification of live newborns. Antioquia-Colombia.

Newborn	N=494	Frequency % (CI95%)
Anthropometric data		
Weight (g)		3225.5 ± 409,2[a]
Head circumference (cm)		Me: 34 (33; 35)[b]
Height (cm)		Me: 50 (49; 51)[b]
Gender		
Female	231	46.8% (42.5–51.0)
Male	263	53.2% (49.0–57.5)
Weight classification WHO[c,d]		
Low birthweight	15	3.0% (1.6–4.7)
Insufficient weight	116	23.5% (19.6–27.5)
Normal	348	70.5% (66.0–74.3)
Macrosomic	15	3.0% (1.6–4.7)
Fenton classification[e]		
Adequate	15	83.3% (62.5–100)
Large for gestational age	3	16.7% (0.0–36.3)
Gestational age	494	Me: 39 (38; 40)[b]

[a] Data are shown as arithmetic mean ± standard deviation; [b]Data are shown in Me: median (lower quartile; upper quartile); [c]World Health Organization; [d] Based on the Public Health Surveillance Protocol, low birth weight at term code 110, 2016.[4]; [e]Based on the Fenton classification.[18]

Table 3

Ratio of maternal hemoglobin by gestation trimester and delta of hemoglobin with birthweight, Antioquia-Colombia.

	Weight <3000 (g) (N=131)	Weight 3000-4000 (g) (N=348)	p[a]	[b]Effect size (CI95%)
HbM in first trimester (g/dL)	13.0 (1.1) n=79	12.8 (1.4) n = 224	0.093	0.44 (0.183–0.697)
HbM second trimester (g/dL)	11.8 (1.1) n = 60	11.9 (1.6) n = 138	0.855	0.49 (0.187–0.793)
HbM third trimester (g/dL)	12.1 (1.2) n = 103	11.8 (1.6) n = 262	0.029	0.43 (0.202–0.658)
HbM DELTA first trimester *vs* third (g/dL)	0.85 (1.2) n = 62	0.9 (1.3) n = 165	0.930	0.50 (0.208–0.792)

Data are shown as median (interquartile range); [a] Mann–Whitney U; [b] Effect size: probability of superiority (PS).

Table 4

Hemoglobin concentration, body mass index, and some maternal gynecology and obstetrics characteristics according to birthweight, Antioquia-Colombia.

	Weight <3000 (g)	Weight 3000-4000 (g)	Value *p* adjusted[a] (PR: CI95%)	Effect size Eta squared[b]
HbM first trimester[c] (g/dL)	13.0 (1.1)	12.8 (1.3)	0.494 (1.08: 0.87–1.33)	0.0023
HbM third trimester[c] (g/dL)	12.1 (1.2)	11.8 (1.6)	0.164 (1.18: 0.93–1.50)	0.0007
Age[c] (years)	21 (7)	22 (8)	0.255 (0.97: 0.91–1.02)	0.0004
BMI[d] pregestational[c]	22.8 (3.1)	23.3 (3.2)	0.043 (0.90: 0.81–0.99)	0.0287
BMI[d] from the last prenatal examination[c]	27.3 (3.3)	27.2 (3.1)	0.497 (0.96: 0.87–1.07)	0.0045
Previous pregnancies n (%)	67 (25.6%)	195 (74.4%)	0.908 (0.95: 0.40–2.25)	0.0038
Previous history of abortions n (%)	27 (32.1%)	57 (67.9%)	0.232 (1.55: 0.75–3.20)	0.0052
Previous deliveries n (%)	54 (24.4%)	167 (75.6%)	0.988 (0.99: 0.44–2.22)	0.0036
UTI n (%)[e]	9 (45.0%)	11 (55.0%)	0.011 (2.53: 1.24–5.18)	0.0014

Delta: It does not apply because of collinearity; [a] Poisson regression of multivariate robust variance; [b]Effect size for a multiple linear regression model (dependent variable birthweight in grams); [c]Median (Interquartile range); [d] Body mass index; [e]Urinary tract infection.

other groups, even when this relationship did not reach statistical significance. The researchers did not apply the ES in their results. This study explored the effect of the change, or the difference (delta), between the HbM in the first and third trimesters on the BW and found that this was medium and important. From the point of view of biological plausibility, HbM must have important physiological changes that help to support maternal and fetal health; therefore, for a healthy pregnancy, it is important and advisable to redefine the cut-off points and normal ranges, as well as the difference that this protein presents, according to the gestation trimester. The inconsistent results of some studies on the relationship between HbM and BW[23] can be attributed to the treatment of the HbM variable in analysis as a result of not defining the trimester in which it was taken, as well as evaluating the HbM in order to define when anemia is present or absent and evaluating its relationship with the BW. In contrast, some investigations establish different cut-off points to define anemia in pregnancy. There are also studies with intervening confounding variables, without statistical treatment, which can bias the relationship between HbM and BW.[14,27]

In a study in Colombia that applied a multivariate regression model, the pre-pregnancy BMI showed a significant relationship with the BW (less than 3,000g and between 3,000 and 4,000g);[14] however, this study only included women with adequate or overweight pre-pregnancy weight. By contrast, a relationship was found between mothers with a treated UTI and neonates weighing less than 3,000g. Some research[28] has shown that these infections can negatively affect the BW, particularly when the mother does not receive timely treatment. It is worth clarifying that a significant number of mothers had UTI but were being treated.

This study showed an increase in anemia as gestation advanced,13 anemic pregnant women in the first trimester, 23 in the second, and 81 in the third, and showed low timely follow-up of their progress given the prevalence of some mothers with anemia during the entire gestation and poor control in avoiding the high number of new cases at the end of the pregnancy; a study carried out by Rahmati *et al.*[29] also reported an increase in anemia at the end of pregnancy attributable to higher fetal demand, the low intake and bioavailability of iron in the maternal diet, and inadequate supplementation. Currently, Colombia has the Comprehensive Maternal-Perinatal Health Care Route[30] for prenatal care of mandatory compliance, which requires the HbM to be determined at three moments of gestation. However, at the date of this study and in the current prenatal records, only two readings are required, before and after the 20th week of pregnancy; notwithstanding the aforementioned, this study and those conducted by others based on this context show that there is a lack of HbM monitoring from a maternal-fetal health point of view. It is necessary to prioritize cost-effective measures to maintain maternal health and not just monitor the HbM in order to diagnose gestational anemia. Given the clinical significance of HbM during pregnancy, it is important to evaluate and monitor it in

the different gestation trimesters and to strive for an adequate concentration that favors maternal and neonatal health and an adequate BW. This study found that the increase in pre-pregnancy BMI reduced the risk of having neonates weighing less than 3,000g and the presence of a UTI, even if it had been treated, increased this probability. The influence of pre-pregnancy maternal weight[6] and the presence of infections on pregnancy[7] have been reported in several studies.

The main limitation of the study is that not all mothers had their HbM measured in each trimester, which could affect the sample size to establish the correlation. The Colombian health system requires only two HbM readings to be taken i.e., before and after the 20th week of pregnancy.

In conclusion, studies on the relationship between HbM during pregnancy and BW have evaluated the statistical significance; however, to date, there are no known investigations that have determined the ES.

HbM is a low-cost, easy-to-determine indicator of iron status and a proxy for maternal nutritional status; therefore, its evaluation and follow-up during pregnancy is necessary in order to guarantee main-

taining adequate concentrations that promote maternal-fetal health and contribute to the adequate BW. HbM monitoring and timely treatment are required to prevent anemia, especially because the risk of anemia increases as gestation progresses.

Other maternal factors, such as pre-pregnancy weight and preventing infection during pregnancy, must be taken into account to promote an adequate BW.

Author's contribution

Madrid-Pérez C: conception, final writing, revision, methodology, research, administration. Restrepo-Mesa SL: revision, research. Ospina AC: revision. Tirado JA: methodology, research. Sierra DCL: methodology, research. Parra-Sosa BE: conception, final writing, revision, methodology, research. All authors approved the final version of the article.

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