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Dynamic Impact of Anemia at Different Gestation on Fetal Low Birth Weight

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Abstract

Objective: To elucidate the impact of anemia and verify the positive effect of normalization of maternal hemoglobin in the third trimester on term fetal birth weight.

Design: Retrospective cohort study
Setting: Community Hospital
Population: Women who gave birth at the author's institution from January 2010 to December 2016

Methods: Maternal blood drawn during the first trimester was compared with that obtained in the third trimester before delivery or scheduled cesarean sections. Those with and without anemia throughout the whole gestation, with anemia during the first trimester only, and with anemia at the time of delivery only were compared. Main Outcome Measures: Rate of term low fetal birth weight

Results: Between January 1, 2010 and December, 2016, a total of 4696 women gave birth at Tung's Taichung MetroHarbor Hospital. Of them, 4290 (91.3%) were without anemia throughout gestation (Group 1), 35 had anemia in the first trimester only (Group 2), 326 had anemia only in the third trimester (Group 3), and 45 had anemia throughout the whole gestation (Group 4). The adjusted odds ratio for giving birth to a full-term baby with low birth weight (< 2500 g) was 3.23 (confidence interval, 1.139-9.404) in Group 4 and 1.594 (confidence interval, 0.482-5.271, P < 0.028) in Group 2.

Conclusions: Gestational anemia is a major detrimental factor for term fetal low birth weight, normalization of anemic status in the third trimester may negate this influence.

Keywords: Anemia, Gestation; Low birth Weight

Introduction

According to the World Health Organization (WHO), the global prevalence of anemia in pregnant women is 38%, with a greater prevalence in developing countries [1,2]. Anemia during pregnancy is a major contributor to both maternal and fetal morbidity; Iron deficiency is a major cause of anemia, in addition to deficiencies in folic acid, Vitamin B12, and inflammation as well as thalassemia during pregnancy [3-8]. Normalization of anemic status through dietary supplementation can reverse the adverse effects on obstetric and neonatal outcomes, as demonstrated in a previous study in which iron supplementation through either oral or parenteral routes exhibited positive effect [9]. This study aimed to address the impact of dynamic changes of serum hemoglobin level through different trimesters on term fetal low birth weight and verify the positive effect of normalization of gestational anemia in the third trimester on fetal birth weight.

Materials and methods

From January 1, 2010 to December 31, 2016, a total of 4696 mothers gave birth at Tung's Taichung MetroHarbor Hospital. We conducted a retrospective analysis of a prospective, population-based cohort from the institutional database, which constituted the target population. The study was approved by the Institutional Review Board (IRB) of our institution (106092). Owing to the retrospective nature of the study, the requirement for obtaining written informed consent from the patients was waived by the IRB. Information regarding maternal demographics, pre-pregnancy comorbidities and gestational morbidity, preterm birth, and fetal birth weight was collected. The hemoglobin levels in maternal blood drawn initially during the first antenatal visits (before the gestational age of 12 weeks) and at the maternal ward before vaginal delivery or planned cesarean section were obtained to allow direct comparison between the first and third trimesters and evaluation of fetal low birth weight in relation to dynamic changes in serum hemoglobin levels. Mothers without complete two-stage hemoglobin data, or with multiple gestations were excluded.

With reference to the WHO guidelines, anemia was defined as a serum hemoglobin level < 11 g/dL in the first trimester and < 10.5 g/dL in the third trimester. The study cohort was categorized into four groups according to the dynamic changes in serum hemoglobin level across the trimesters, with Group 1 comprising those without anemia throughout the gestation Group 2, those who were anemic only in the first trimester; Group 3, those who were anemic only in the third trimester; and Group 4, those with anemia throughout the gestation.

The main endpoint was term (> 37 gestational weeks) fetal birth weight, and those weighing < 2500 g were defined as low birth weight. Descriptive statistics were employed to describe the demographic variables, while continuous variables were expressed as mean with standard deviations. Categorical variables were expressed numerically as percentages. Multivariate logistic regression analysis was performed to

identify potential risk factors for anemia and delivery outcomes (preterm birth and low birth weight). The association between hemoglobin levels and delivery outcomes was analyzed; and three different logistic regression models were established: Group 1 versus Groups 2, 3, and 4. For the logistic regression model with Group 1 versus Group 4, a crude odds ratio and adjusted odds ratio with 95% confidence intervals (CIs) were calculated after adjusting for maternal age, parity, pre-pregnancy co-morbidities, and gestational complications. All statistical analyses were performed using SPSS 22.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

A total of 4696 mothers gave birth at Tung's Taichung MetroHarbor Hospital during the study period, and they were categorized as follows: Group 1, 4290 women; Group 2, 35 women; Group 3, 326 women; and Group 4, 45 women. The mean maternal age was 30.04 years; 2416 (51.4%) and 2166 (46.1%) of the participants were primigravida and multigravida, respectively, while 114 (2.4%) participants had undocumented parity, with an even distribution among the four groups. Cesarean delivery was performed in 1769 (37.7%) mothers, 2881 (61.4%) gave birth through spontaneous vaginal route, and 46 (1.0%) underwent operative delivery. The cesarean delivery rates in Groups 1-4 were 37.2%, 37.1%, 42.8%, and 44.4%, respectively, with no significant intergroup differences. The rates of pre-pregnancy comorbidities such as diabetes mellitus, hypertension, congenital heart disease, previous history of pre-eclampsia and eclampsia, and renal hydronephroses were evenly distributed among the four groups (Table 1). Gestational hypertension was noted in 13.3%, 17.1%, 11.6%, and 15.6% of the participants from Groups 1-4, respectively, with no statistically significant intergroup differences. The overall rate of low birth weight at term was 5.8%, with Groups 1-4 showing rates of 5.6%, 8.6%, 7.2%, and 13.3%, respectively (Table 1). The overall maternal prevalence of anemia in the study cohort during the study period was 8.5%, while the prevalence of anemia in the first and third trimesters were 1.7% and 7.7%, respectively.

Table 1: Patient Demographic

	Total (n = 4,696)	Group 1 (n = 4290)[c]	Group 2 (n = 35)[c]	Group 3 (n = 326)[c]	Group 4 (n = 45)[c]
Maternal age (Mean ± SD; years)	30.04 ± 4.337	30.1 ± 4.248	31.23 ± 5.320	29.25 ± 5.038	28.6 ± 5.840
Parity					
0, n (%)	2416 (51.4)	2232 (52.0)	20 (57.1)	148 (45.3)	16 (35.6)
1, n (%)	1650 (35.1)	1493 (34.8)	9 (25.7)	129 (39.5)	19 (42.2)
≥ 2, n (%)	516 (11.0)	457 (10.6)	5 (14.3)	45 (13.8)	9 (20.0)
Unknown or unavailable	114 (2.5)	108 (2.6)	1 (2.9)	4 (1.4)	1 (2.2)
Mode of delivery					
Caesarean section	1769 (37.7)	1598 (37.2)	13 (37.1)	138 (41.7)	20 (44.4)
Normal spontaneous delivery	2875 (61.2)	2651 (61.8)	22 (62.9)	177 (54.3)	25 (55.6)
Instrumental vaginal delivery	52 (1.1)	41 (1.0)	0 (0.0)	11 (4)	0 (0.0)
Maternal comorbidities					
Diabetes mellitus	40 (0.9)	38 (0.9)	0 (0.0)	1 (0.3)	1 (2.2)
Hypertension	23 (0.5)	19(0.4)	0 (0.0)	3 (0.9)	1 (2.2)
Congenital heart disease	34 (0.7)	27 (0.6)	0 (0.0)	6 (1.9)	0 (0.0)
History of pre-eclampsia	14 (0.3)	12 (0.3)	0 (0.0)	2 (0.6)	0 (0.0)
History of eclampsia	1 (0.01)	1 (0.01)	0 (0.0)	0 (0.0)	0 (0.0)
History of hydronephrosis	13 (0.3)	11 (0.3)	1 (2.9)	1 (0.3)	0 (0.0)
Anemia	54 (1.0)	31 (0.7)	2 (5.7)	11 (3.5)	10 (22.2)
Gestational comorbidities					
Diabetes mellitus	35 (0.7)	31 (0.7)	0 (0.0)	2 (0.6)	2 (2.2)
Hypertension	29 (0.6)	28 (0.7)	0 (0.0)	0 (0.0)	1 (2.2)
Heart disease	6 (0.1)	6 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Pre-eclampsia	59 (1.3)	52 (1.2)	0 (0.0)	7 (2.2)	0 (0.0)
Eclampsia	52 (1.1)	52 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
Hydronephrosis	7 (0.1)	7 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Anemiab	34 (0.7)	16 (0.4)	0 (0.0)	14 (4.4)	4 (8.9)
High blood pressure (> 140/90 mmHg)					
High blood pressure in first trimester	55 (1.2)	51 (1.2)	0 (0.0)	3 (0.9)	1 (2.2)
High blood pressure in third trimester	622 (13.2)	571 (13.3)	6 (17.1)	37 (11.6)	8 (15.6)
Pregnancy outcomes					
Preterm birth	324 (6.9)	290 (6.8)	2 (5.7)	29 (9.1)	3 (6.7)
Low birth weight	271 (5.8)	239 (5.6)	3 (8.6)	23 (7.2)	6 (13.3)
Multiple birth	56 (1.2)	40 (0.9)	0 (0.0)	14 (4.4)	2 (4.4)

[a]Data are expressed as means ± standard deviations (SDs) or n (%)
[b]Anemia is defined as hemoglobin < 11 g/dL (first trimester) and < 10.5 g/dL (third trimester)
[c]According to the hemoglobin levels, patients were divided into 4 groups:
Group 1: Non-anemic in both first and third trimesters
Group 2: Anemic in first but not third trimester
Group 3: Non-anemic in first but anemic in third trimester
Group 4: Anemic in both first and third trimesters

The crude ratio for giving birth to a low-birth-weight baby at term (< 2500 g) among mothers with anemia throughout the whole gestation was 2.443 (1.022-5.840), and after adjusting this ratio for maternal age, parity, pre-pregnancy comorbidities, and gestational comorbidity, the odds ratio for giving birth to a low-birth-weight baby at term was 3.273 (1.139-9.404; p = 0.028 (Table 2).

For those with first-trimester anemia but normalized at the third trimester, the odds ratio for giving birth to a term low-birth-weight baby was 1.594 (0.482-5.31) (Table 2).

Table 2: Association between anemia and pregnancy outcomes

	Anemic in first trimester only	**Anemic in third trimester only**	**Anemic in both first and third trimesters**
Delivery outcomes	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Age			
< 35 years	1	1	1
> 35 years	1.996 (0.931-4.280)	1.000 (0.726-1.379)	0.887(0.374-2.104)
Preterm birth			
No	1	1	1
Yes	0.835 (0.199-3.496)	1.392 (0.933-2.076)	0.984 (0.303-3.193)
Low birth weight	1	1	1
No	1	1	1
Yes	1.594 (0.482-5.271)	1.294 (0.829-2.019)	2.499* (1.044-5.979)

Delivery outcomes	**Crude OR(95% CI)**	**P**	**Adjusted OR(95% CI)**	**P**
Preterm birth		0.948		0.386
No	1		1	
Yes	0.962 (0.296-3.120)		0.537 (0.132-2.188)	
Low birth weight		0.045*		0.028*
No	1		1	
Yes	2.443 (1.022-5.840)		3.273 (1.139-9.404)	

*P < 0.05. CI, confidence interval.

Discussion

This study demonstrated the dynamic impact of maternal anemia on term fetal birth weight across trimesters, with adjusted odds ratio of 3.42 in women with anemia throughout the gestation giving birth to a low-birth-weight baby. Interestingly, this study also revealed that women who had anemia in their first trimester with subsequent normalized hemoglobin levels by the third trimester were not at risk of giving birth to a low-birth-weight term baby (OR, 1.594; CI, 0.482-5.271), corroborating the previously reported modifiable nature of gestational anemia in prevention of preterm delivery and low birth weight. Although previous studies have demonstrated the causative effects of anemia on fetal birth weight as well as preterm delivery, this study did not show an effect of anemia on preterm birth, which might be partially attributable to the easily accessible health system and the small study population.

The strength of this study lies in the comprehensive follow-up of a large cohort of mothers with complete documentation of demographic data as well as serum hemoglobin data obtained at first and third trimesters, which constituted a robust database for analysis. However, the study had inherent limitations of the nature of retrospective studies with analysis of data from a single institution, making the generalizable of this notion somewhat limited. Moreover, the fact that anemia in this study was arbitrarily attributed to iron deficiency without verification with either serum ferritin or transferrin saturation constituted another major limitation of this study, albeit presumably the majority of anemia cases during pregnancy could be attributable to iron-deficiency anemia and modifiable through iron supplementation.

Early detection of maternal anemia, specifically in those with iron-deficiency anemia, should be a routine practice at first antenatal visits. Women with anemia should receive appropriate consultation to correct with either iron supplementation or vitamins / folic acids accordingly in order to negate the impact of anemia on fetal birth weight [10,12,13]. Persistent maternal anemia throughout all trimesters has a detrimental effect on term fetal birth weight, and the majority of this can be modified through iron supplementation during pregnancy.

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Ethics approval: The study design was approved by the ethics review board at Tung's Taichung MetroHarbor Hospital on February 1,2018 with IRB # 106092, waiving informed consent from the study population.

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