

Changes in Maternal Hemoglobin Concentration and Risk of Low Birth Weight and Small-for-Gestational-Age in the United Arab Emirates: The Mutaba'ah Study

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Background: Maternal hemoglobin (Hb) concentration and changes in Hb across trimesters have been linked to low birth weight (LBW) and small-for-gestational-age (SGA). However, these associations have shown inconsistent results and have not been investigated in pregnant women in the United Arab Emirates (UAE). We investigated the association between changes in Hb concentration during the first and second trimesters and birth weight, LBW, and SGA among pregnant women in the UAE.

Methods: We utilized data from the Mutaba'ah Study. Change in Hb was computed as the difference between the first and second trimester Hb concentrations. LBW and SGA were defined as birth weight below 2500 grams and birth weight below the 10th percentile, respectively. Multivariable regression models were used to investigate the association between changes in maternal Hb and birth weight, LBW and SGA.

Results: A total of 1500 pregnant women were included. The mean maternal age was 32 years (SD 6). Overall, Hb concentration declined from the first to the second trimesters by a median of -9 g/L (IQR: -14, -3). LBW and SGA were observed among 6% and 10% of the newborns, respectively. Pregnant women who experienced the least reduction or an increase in Hb concentration had a higher risk of both LBW (adjusted odds ratio [aOR]: 3.43, 95% confidence interval [CI]: 1.77 to 6.96) and SGA (aOR: 2.08, 95% CI: 1.28 to 3.40) compared to those with the greatest reduction in Hb concentration.

Conclusion: Minimal reductions in Hb levels from the first to the second trimester were associated with LBW and SGA. The average Hb levels during the second trimester were inversely associated with birth weight and SGA. Monitoring variations in maternal Hb early in pregnancy may enhance the early identification of pregnancies at risk.

Keywords: hemoglobin, Hb change, birthweight, SGA, pregnancy

Introduction

Changes in maternal hemoglobin (Hb) concentration during pregnancy are a well-recognized physiological adaptation to support fetal growth.¹ This change is primarily driven by maternal hemodynamic adaptation, in which plasma volume expansion results in a relative reduction in Hb concentration. The relationship between maternal Hb concentration and pregnancy outcomes has been a topic of significant debate and controversy in maternal and child health research.² Previous studies have found different links between maternal Hb levels and adverse birth outcomes, such as low birth weight (LBW) and small-for-gestational-age (SGA). Some studies showed that low Hb concentration (<110 g/L) is associated with

a higher risk of LBW,^{3–6} while others suggest that high Hb levels (≥ 130 g/L) may also increase the risk.^{7–9} Some reports describe a U-shaped association,^{10–12} whereas others found no such association.^{13–15}

Recent evidence suggests that the timing of Hb measurement during pregnancy influences the relationship with birth outcomes, with low Hb in the first trimester being more strongly linked to adverse outcomes, while high Hb poses risks throughout pregnancy.^{16,17} Moreover, associations between changes in maternal Hb levels – from early to late pregnancy – and the risks of adverse birth outcomes, including LBW and SGA deliveries, have also been reported linked to fetal growth outcomes. Studies from multiple countries have shown that minimal Hb reduction during pregnancy increases the likelihood of delivering LBW and SGA infants.² Studies from multiple countries have shown that minimal Hb reduction during pregnancy increases the likelihood of delivering LBW and SGA infants.^{18,19}

Although studies from other countries have established a link between changes in maternal Hb levels and LBW and SGA infants, it is uncertain whether similar risks are present in the United Arab Emirates (UAE) population, given the high prevalence of obesity and the swift alterations in lifestyle and nutritional habits that may affect anemia and fetal outcomes. Furthermore, there is insufficient direct evidence regarding the overall prevalence of anemia in pregnant women and LBW in the UAE. Prior research indicated that 25% of Emirati women aged 15 to 49 years are anemic, and LBW prevalence ranging from 9% to 11%.^{20–23} One study among pregnant women in the UAE examined trends in maternal Hb levels, but did not investigate adverse outcomes associated with these changes.²⁴ In the present study, we assessed the association between changes in maternal Hb concentration and the risk of LBW and SGA infants in a cohort of pregnant women in the UAE.

Methods

Study Design, Setting and Participants

This analysis used data from the Mutaba'ah Study, a large ongoing prospective birth cohort in Al Ain, UAE, that investigates maternal and child health. Ethical approval for the Mutaba'ah Study was obtained from the Human Research Ethics Committee of the United Arab Emirates University (ERH-2017-5512) and the Abu Dhabi Health Research and Technology Ethics Committee (DOH/CVDC/2022/72). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, and participants enrolled voluntarily after providing informed consent.

All pregnant women from the Emirati population, aged 18 or older, living in Al Ain City who can provide informed consent are eligible to participate in the Mutaba'ah Study. Data were collected through questionnaires and medical record linkage. More detailed information about the Mutaba'ah Study can be found elsewhere.²⁵ This analysis includes pregnant women recruited in the Mutaba'ah Study who gave birth between October 2017 and June 2024. Women with multiple pregnancies, preterm deliveries, and those with missing hemoglobin measurements in the first or second trimesters of pregnancy, birth outcome data, or gestational age were excluded from the analysis.

Variables and Measurements

Maternal educational level was categorized based on the responses to the self-administered questionnaire as “Higher than secondary” (Vocational/Diploma, Bachelors, Masters or Doctorate) or “Secondary or lower” (Illiterate, Never attended school, Primary or Secondary). Hemoglobin concentration was measured as part of routine antenatal care and recorded in the medical records of participating healthcare facilities. All available measurements of Hb concentration (g/L) during the pregnancy were extracted from the medical records. Data on maternal age (years), parity, early-pregnancy body mass index (BMI) (first available BMI recorded within the first trimester), pre-existing diabetes status (Yes/No), pre-existing hypertension status (Yes/No), delivery mode (vaginal/caesarean), fetal sex (male/female), gestational age at birth (weeks) and birth weight (grams), were also extracted from the medical records.

Hb concentration of the first 12 weeks of gestation (first trimester) and second 12 weeks of gestation (second trimester) was estimated as the average of all available Hb measurements within each trimester. Birth weight less than 2500 grams was defined as low birth weight (LBW). Small-for-gestational-age (SGA) was defined as a birth weight below the 10th percentile using the reference reported by INTERGROWTH-21st Project.²⁶ The INTERGROWTH-21st International Standard for Newborn Weight is the most suitable available birth weight reference because it is globally

representative, incorporating data from various regions and countries, including Oman, a neighboring country to the UAE.

Post-Hoc Sample Size Estimation

The minimum required sample size for developing the multivariable linear regression model with birth weight as the outcome was retrospectively estimated using the approach of Riley et al for continuous outcomes²⁷ We used the adjusted $R^2=0.07$; conservative estimate of anticipated model performance, from a published multivariable linear regression of birth weight on maternal hemoglobin and related predictors from the region.²⁸ The average (SD) birth weight was approximated from the same study, and we allowed a multiplicative margin of error of 1.10 for estimation of the intercept and residual standard deviation. Specifying 10 candidate predictor parameters, yielded a recommended minimum sample size of $N= 964$ participants for new model development.

Data Analysis

Change in Hb concentration was computed as the difference between the average Hb concentrations during the first and second trimesters for each pregnant woman. To facilitate easy comparison, the change in Hb was further divided into tertiles – three equal cut-offs comprising those with the *greatest reduction* (Tertile 1), those with a *moderate reduction* (Tertile 2), and those with the *least reduction or an increase in Hb concentration* (Tertile 3).

Categorical variables were summarized using frequencies and percentages. The mean and standard deviation (SD; Range) were used to summarize continuous variables, except for the difference in Hb concentration, which was summarized as median and interquartile range (IQR; Range) due to skewed distribution.

Associations between Hb change tertiles and categorical variables were analyzed using Pearson's chi-squared test for trends. The relationship between Hb change tertiles and quantitative variables was evaluated with Kruskal–Wallis ANOVA. Linear regression models were used to examine the relationship between Hb levels in the first and second trimesters and birth weight. Logistic regression was used to assess the associations of Hb change (both continuous and tertile measures) and first- and second-trimester Hb levels with LBW and SGA. For each analysis, a crude model and two adjusted models were constructed. In the first adjusted model (A), adjustments included maternal age, early-pregnancy BMI, and parity. Additionally, first-trimester Hb levels were controlled for when examining the association between Hb change and the three outcomes. In the second adjusted model (B), adjustments included all variables from Model A, as well as pre-existing diabetes mellitus and pre-existing hypertension. As part of a sensitivity analysis, additional models were developed to explore the potential confounding effect of first-trimester Hb on the relationship between second-trimester Hb and birth weight, LBW, and SGA.

R software (version 4.4.1) was used for data analysis. All statistical tests were performed at the 5% significance level.

Results

Hb Concentration Change

A total of 1500 pregnant women were included in the study (Table 1). The average Hb concentrations during the first and second trimesters were 115 g/L (SD: 11 g/L; range: 75 to 147) and 107 g/L (SD: 10 g/L; range: 70 to 139), respectively. Overall, the change in Hb was estimated at -9 g/L (IQR: -14 to -3 ; range: -34 to 31). The average Hb changes for Tertile 1, Tertile 2, and Tertile 3 were -16 g/L (IQR: -20 to -14 ; range: -34 to -12), -8 g/L (IQR: -10 to -7 ; range: -12 to -5), and 0 g/L (IQR: -3 to 4 ; range: -5 to 31), respectively (Table 1 and Figure 1).

Demographic, Clinical, and Obstetric Characteristics

The mean age of the women was 32 years (SD: 6; range: 18 to 52); 76% were multiparous, and about half (51%) had completed higher education. About two-thirds of the women (67%) were overweight or obese, 8% had pre-existing diabetes mellitus, and 6% had pre-existing hypertension. The overall mean gestational age was 38.9 weeks (SD: 1.17; range: 37 to 43), and just over half (52%) of the newborns were male. The change in Hb was not statistically significantly different across these characteristics, except for education levels ($p<0.001$) (Table 1).

Table 1 Association Between Sociodemographic, Comorbidities, and Pregnancy and Neonatal Outcomes by Tertiles of Hb Concentration Changes from First to second Trimester

	All	Hb Change Tertiles			p-value
		Tertile 1	Tertile 2	Tertile 3	
Range (g/L)		-34 to -12	-12 to -5	-5 to 31	
N (%)	1500	521 (34.7%)	498 (33.2%)	481 (32.1%)	
1st trimester Hb, mean (SD); Range	115 (11) 75, 147	121 (10) 90, 147	116 (10) 80, 146	109 (11) 75, 143	<0.001
2nd trimester Hb, mean (SD); Range	107 (10) 70, 139	103 (9) 70, 125	108 (10) 73, 136	111 (10) 80, 139	<0.001
Hb change, median (IQR)	-9 (-14, -3)	-16 (-20, -14)	-8 (-10, -7)	0 (-3, 4)	<0.001
Maternal age, mean (SD); Range	32 (6) 18, 52	32 (6) 18, 52	32 (6) 18, 47	32 (6) 19, 46	0.900
Education level					<0.001
Higher than secondary	722 (51%)	230 (48%)	277 (59%)	215 (47%)	
Secondary or lower	680 (49%)	251 (52%)	190 (41%)	239 (53%)	
Early-pregnancy BMI					0.800
Normal	487 (33%)	174 (34%)	152 (31%)	161 (34%)	
Overweight	499 (34%)	175 (34%)	167 (34%)	157 (33%)	
Obese	485 (33%)	162 (32%)	168 (34%)	155 (33%)	
Pre-existing diabetes					0.400
No	1375 (92%)	478 (92%)	462 (93%)	435 (90%)	
Yes	125 (8%)	43 (8.2%)	36 (7%)	46 (10%)	
Pre-existing hypertension					0.600
No	1407 (94%)	492 (94%)	468 (94%)	447 (93%)	
Yes	93 (6%)	29 (6%)	30 (6%)	34 (7%)	
Parity					0.300
0	361 (24%)	114 (22%)	131 (26%)	116 (24%)	
≥1	1139 (76%)	407 (78%)	367 (74%)	365 (76%)	
GA at birth (weeks), mean (SD); Range	38.94 (1.17) 37–43	38.97 (1.15) 37–42	38.94 (1.17) 37–42	38.90 (1.19) 37–43	0.700
Baby gender					0.300
Female	726 (48%)	265 (51%)	238 (48%)	223 (46%)	
Male	774 (52%)	256 (49%)	260 (52%)	258 (54%)	
Birth weight (g), mean (SD); Range	3130 (407) 1620–4458	3173 (394) 1960–4380	3134 (402) 2065–4458	3081 (422) 1620–4260	0.007

(Continued)

Table 1 (Continued).

	All	Hb Change Tertiles			p-value
		Tertile 1	Tertile 2	Tertile 3	
Low birth weight					<0.001
No	1411 (94%)	507 (97%)	464 (93%)	440 (92%)	
Yes	89 (6%)	14 (3%)	34 (7%)	41 (8%)	
Small-for-gestational age					<0.001
No	1355 (90%)	486 (93%)	454 (91%)	415 (86%)	
Yes	144 (10%)	35 (7%)	44 (9%)	65 (14%)	

Note: Bolded p-values indicate statistical significance at 5% level.

Abbreviations: Hb, maternal hemoglobin; BMI, Body Mass Index; GA, gestational age; IQR, Interquartile range; SD, Standard deviation.

The median birth weight was 3130 grams (SD: 407; range: 1620 to 4458), with 6% classified as LBW and 10% as SGA. The mean birth weight of babies born to women in Tertile 3 was significantly lower than that of babies born to women in Tertile 1 and Tertile 2 of Hb change ($p=0.007$). Similarly, the proportions of LBW differed significantly across the tertiles of Hb change ($p<0.001$), with the highest in Tertile 3 (8%), followed by Tertile 2 (7%), and Tertile 1 (3%). The proportions of SGA also varied significantly ($p<0.001$) across the Hb change tertiles: 14% in Tertile 3, 9% in Tertile 2, and 7% in Tertile 1 (Table 1).

Association Between Hb Changes and Birthweight-Related Outcomes

There was a significant ($p<0.001$) difference in the mean change in Hb between deliveries with and without LBW and SGA (Figure 2A and B; respectively). A one g/L increase in Hb from the first to the second trimester was associated with

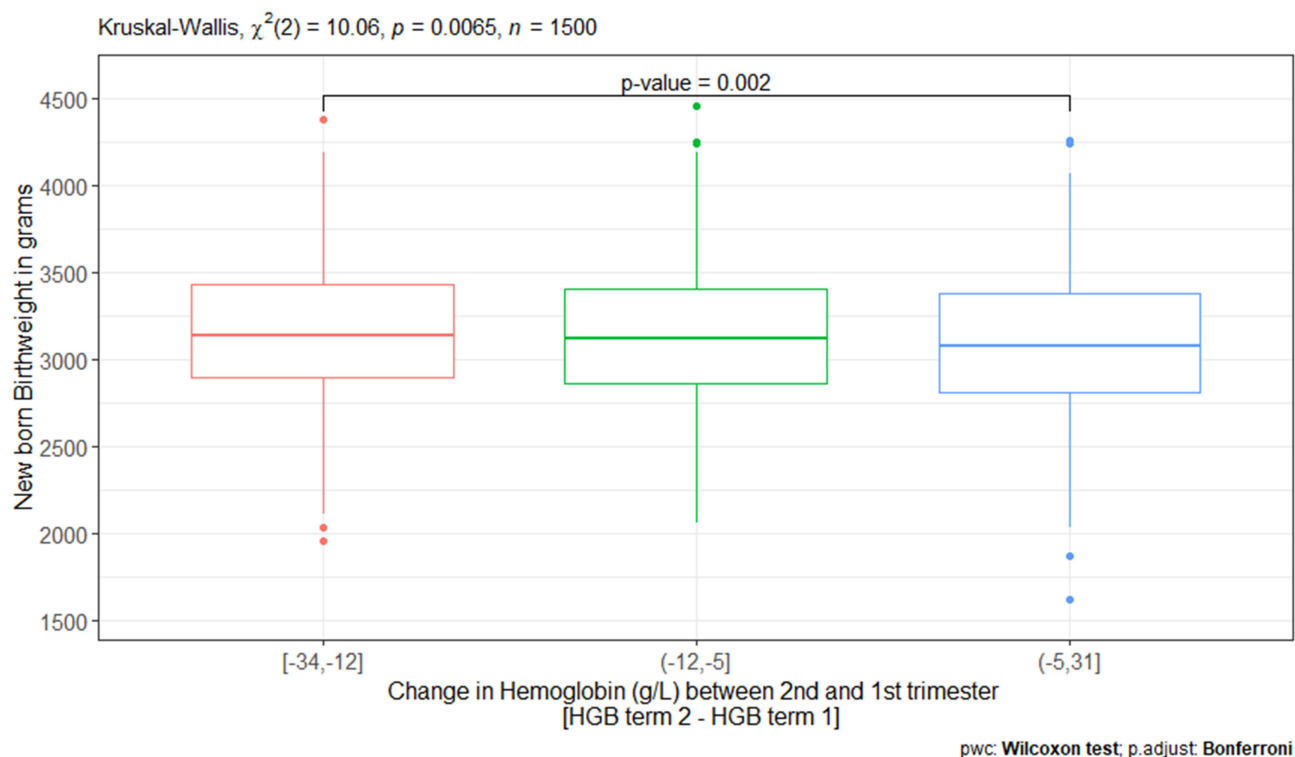


Figure 1 Distribution of birth weight by tertiles of Hb change from the first to the second trimester.

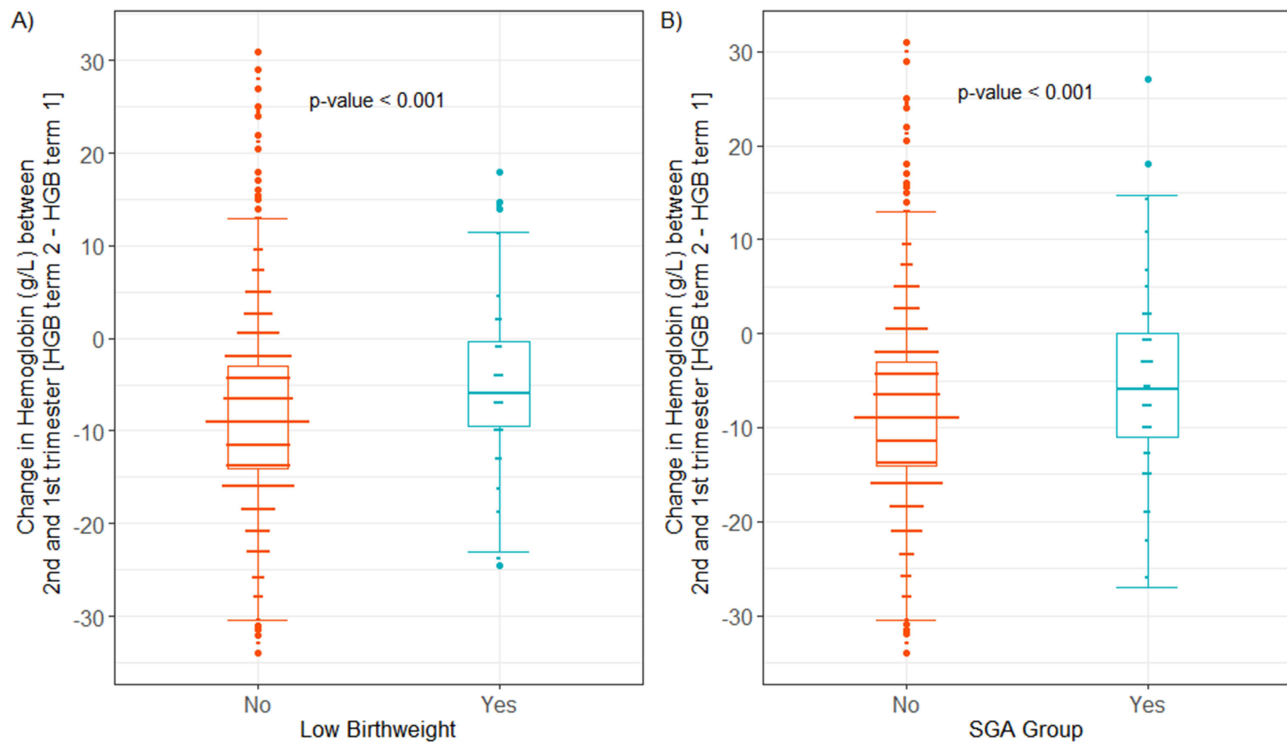


Figure 2 Distribution of Hb changes from the first to the second trimester by (A) low birth weight and (B) Small-for-gestational-age (SGA).

a decrease in birth weight by an average of 5.1 grams (β : -5.1 , 95% confidence interval [CI]: -7.8 to -2.5) after adjusting for several potential confounders (Table 2). In terms of the relationship with the Hb change tertiles, babies born to women in Tertile 3 of Hb reduction (*least reduction or an increase in Hb concentration*) had, on average, 84 grams lower birth weight compared with those born to women in Tertile 1 (β : -84 , 95% CI: -138 to -29). Birth weight was not significantly associated with being in Tertile 2 compared to being in Tertile 1 of Hb reduction ($p=0.150$).

Table 2 Linear Regression Analysis for the Relationship Between Hb Concentration and Birth Weight

	Unadjusted Model		Model A*		Model B*	
	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Hb change[†]						
Hb (continuous)	-4.9 (-7.2, -2.5)	<0.001	-5.2 (-7.8, -2.5)	<0.001	-5.1 (-7.8, -2.5)	<0.001
Tertile 1	Reference		Reference		Reference	
Tertile 2	-39 (-89, 11)	0.130	-36 (-86, 14)	0.150	-37 (-87, 13)	0.150
Tertile 3	-92 (-142, -42)	<0.001	-84 (-139, -30)	0.002	-84 (-138, -29)	0.003
First trimester						
Hb (continuous)	1.4 (-0.42, 3.2)	0.130	1.1 (-0.71, 2.9)	0.240	0.97 (-0.83, 2.8)	0.290
Tertile 1	Reference		Reference		Reference	
Tertile 2	8.6 (-41, 58)	0.730	-2.3 (-51, 47)	0.930	-3.5 (-52, 45)	0.890
Tertile 3	51 (0.17, 103)	0.049	42 (-9.2, 93)	0.110	37 (-14, 88)	0.150

(Continued)

Table 2 (Continued).

	Unadjusted Model		Model A*		Model B*	
	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Second trimester						
Hb (continuous)	-1.9 (-3.9, 0.13)	0.066	-2.1 (-4.1, -0.10)	0.039	-2.2 (-4.2, -0.17)	0.034
Tertile 1	Reference		Reference		Reference	
Tertile 2	-50 (-99, -0.16)	0.049	-44 (-93, 4.3)	0.074	-43 (-91, 5.7)	0.084
Tertile 3	-49 (-100, 2.2)	0.061	-51 (-101, 0.05)	0.050	-51 (-102, -0.90)	0.046

Notes: *Model A: Adjusted for maternal age, early-pregnancy BMI, and parity. Model B: Model A + pre-existing diabetes mellitus and pre-existing hypertension. †Model A and Model B are additionally adjusted for Hb in the first trimester. Bolded p-values indicate statistical significance at 5% level.

Abbreviation: Hb, maternal hemoglobin.

When examining the average Hb levels separately for the first and second trimester, there was no significant association between birth weight and average Hb levels in the first trimester. However, a significant association was observed between birth weight and average Hb levels in the second trimester. For each one g/L increase in Hb in the second trimester, birth weight decreased by an average of 2.2 grams ($\beta=-2.2$, 95% CI=-4.2 to -0.17). Compared to women in Tertile 1 of the second trimester Hb, average birth weight was 51 grams lower in Tertile 3 ($\beta: -51$, 95% CI: -102 to -1.90) (Table 2).

The odds of LBW increased by an average of 5% (adjusted odds ratio [aOR]: 1.05, 95% CI: 1.02 to 1.08) for each one g/L increase in Hb (Table 3). Furthermore, being in Tertile 2 (aOR: 2.62, 95% CI: 1.39 to 5.18) and Tertile 3 (aOR: 3.43, 95% CI: 1.77 to 6.96) of Hb reduction were associated with a significant increase in the odds of LBW as compared to those in Tertile 1. Moreover, one g/L increase in average second-trimester, not first-trimester, Hb levels was significantly associated with LBW (aOR: 1.03, 95% CI: 1.01 to 1.05). Additionally, women in Tertile 3 of average second-trimester Hb had almost two times the odds of LBW compared to those in Tertile 1 (aOR: 1.86, 95% CI: 1.07 to 3.31). There was

Table 3 Logistic Regression Analysis for the Association Between Hb Concentration and Low Birth Weight

	Unadjusted Model		Model A*		Model B*	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Hb change[†]						
Hb (continuous)	1.04 (1.02, 1.07)	<0.001	1.05 (1.02, 1.08)	0.001	1.05 (1.02, 1.08)	0.001
Tertile 1	Reference		Reference		Reference	
Tertile 2	2.65 (1.44, 5.17)	0.003	2.61 (1.39, 5.16)	0.004	2.62 (1.39, 5.18)	0.004
Tertile 3	3.37 (1.86, 6.49)	<0.001	3.44 (1.78, 6.98)	<0.001	3.43 (1.77, 6.96)	<0.001
First trimester						
Hb (continuous)	0.99 (0.97, 1.01)	0.400	1.0 (0.98, 1.01)	0.590	1.00 (0.98, 1.02)	0.660
Tertile 1	Reference		Reference		Reference	
Tertile 2	1.10 (0.68, 1.80)	0.690	1.18 (0.71, 1.96)	0.530	1.18 (0.71, 1.98)	0.510
Tertile 3	0.63 (0.35, 1.11)	0.110	0.68 (0.36, 1.22)	0.200	0.71 (0.38, 1.29)	0.270

(Continued)

Table 3 (Continued).

	Unadjusted Model		Model A*		Model B*	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Second trimester						
Hb (continuous)	1.02 (1.00, 1.05)	0.028	1.03 (1.00, 1.05)	0.031	1.03 (1.01, 1.05)	0.027
Tertile 1	Reference		Reference		Reference	
Tertile 2	1.31 (0.75, 2.30)	0.350	1.29 (0.73, 2.31)	0.390	1.25 (0.70, 2.25)	0.450
Tertile 3	1.82 (1.07, 3.16)	0.029	1.85 (1.06, 3.28)	0.032	1.86 (1.07, 3.31)	0.030

Notes: *Model A: Adjusted for maternal age, early-pregnancy BMI, and parity. Model B: Model A + pre-existing diabetes mellitus and pre-existing hypertension. †Model A and Model B are additionally adjusted for Hb in the first trimester. Bolded p-values indicate statistical significance at 5% level.

Abbreviation: Hb, maternal hemoglobin.

no significant difference in the odds of LBW between women in Tertile 2 and those in Tertile 1 of average second-trimester Hb.

A positive association was observed between increased Hb and SGA (Table 4). A one g/L increase in Hb during the second trimester was associated with an average 4% increase in the odds of SGA (aOR: 1.04, 95% CI: 1.01 to 1.06).

Table 4 Logistic Regression Analysis for the Association Between Hb Concentration and Small-for-Gestational-Age

	Unadjusted Model		Model A*		Model B*	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Hb change[†]						
Hb (continuous)	1.04 (1.02, 1.06)	<0.001	1.04 (1.01, 1.06)	0.001	1.04 (1.01, 1.06)	0.001
Tertile 1	Reference		Reference		Reference	
Tertile 2	1.35 (0.85, 2.15)	0.210	1.29 (0.80, 2.09)	0.300	1.30 (0.80, 2.10)	0.290
Tertile 3	2.17 (1.42, 3.38)	<0.001	2.08 (1.28, 3.39)	0.003	2.08 (1.28, 3.40)	0.003
First trimester						
Hb (continuous)	0.99 (0.98, 1.01)	0.250	0.99 (0.98, 1.01)	0.360	0.99 (0.98, 1.01)	0.380
Tertile 1	Reference		Reference		Reference	
Tertile 2	0.99 (0.67, 1.48)	0.980	1.06 (0.71, 1.60)	0.770	1.07 (0.71, 1.61)	0.760
Tertile 3	0.65 (0.41, 1.01)	0.057	0.68 (0.42, 1.09)	0.110	0.70 (0.43, 1.11)	0.130
Second trimester						
Hb (continuous)	1.02 (1.00, 1.03)	0.050	1.02 (1.00, 1.04)	0.060	1.02 (1.00, 1.04)	0.056
Tertile 1	Reference		Reference		Reference	
Tertile 2	1.14 (0.74, 1.76)	0.550	1.08 (0.70, 1.69)	0.730	1.07 (0.69, 1.67)	0.770
Tertile 3	1.41 (0.92, 2.16)	0.120	1.41 (0.90, 2.19)	0.130	1.41 (0.91, 2.20)	0.130

Notes: *Model A: Adjusted for maternal age, early-pregnancy BMI, and parity. Model B: Model A + pre-existing diabetes mellitus and pre-existing hypertension. †Model A and Model B are additionally adjusted for Hb in the first trimester. Bolded p-values indicate statistical significance at 5% level.

Abbreviation: Hb, maternal hemoglobin.

Similarly, women in Tertile 3 of Hb change had twice the odds of SGA compared to those in Tertile 1 (aOR: 2.08, 95% CI: 1.28 to 3.40). On the other hand, there was no significant difference in odds of SGA between women in Tertile 2 and those in Tertile 1 ($p=0.290$). On the other hand, second-trimester Hb was not significantly associated with SGA.

In the supplementary models examining the association between second-trimester Hb and the relevant birth weight outcomes, after additionally adjusting for first-trimester Hb, the results were broadly similar in direction and statistical significance, with only three exceptions ([Supplementary Table 1](#)). Furthermore, a significant association was observed between Tertile 2 of second-trimester Hb and birth weight ($\beta=-71$, 95% CI: -124 to -19 , $p=0.008$) when compared to women in Tertile 1. Additionally, changes in second-trimester Hb were positively associated with SGA (aOR=1.04, 95% CI: 1.01 to 1.06), and women classified within Tertile 3 of second-trimester Hb demonstrated a significantly higher likelihood of having an SGA infant than those in Tertile 1 (aOR: 1.96, 95% CI: 1.14 to 3.38).

Discussion

This study examined changes in Hb concentrations between the first and the second trimesters among pregnant women in the UAE and their association with birth weight and SGA. The findings revealed a decrease in Hb among pregnant women during the second trimester. There were inverse associations between the change in Hb concentration and birth weight and SGA. Additionally, average Hb levels during the second, rather than the first, trimester were inversely associated with birth weight and SGA.

Our finding of an overall decline in Hb concentration during the second trimester is consistent with reports from several earlier studies.^{2,19,29–32} This is attributed to hemodilution, a well-documented phenomenon that occurs during the second trimester as a result of significant plasma volume expansion.^{29,33} A meta-analysis involving 10 studies and 347 pregnancies reported a significant increase in plasma volume during pregnancy as compared to the non-pregnancy state, with the highest volume expansion happening during the second trimester.²⁹

The findings of the present study indicate an inverse association between the change in Hb concentration and birth weight and SGA, with those who experienced a lower reduction or even an increase in Hb having a higher risk of LBW and SGA. This is in agreement with reports in other studies.^{2,19,34,35} Although focusing on Hb changes later in pregnancy, a study among Japanese pregnant women and their newborns found that a smaller reduction in Hb levels during the later stages of pregnancy, as compared to early pregnancy, was significantly associated with LBW.² Similarly, Peng et al, in a more recent study among pregnant women in China, reported that the increase in maternal Hb from the second to the third trimester was positively correlated with both LBW and SGA infants.¹⁹ In 2022, a study involving two large cohorts of pregnant women in the United Kingdom reported that higher maternal Hb in late pregnancy, which may signify a lower increase from early pregnancy, was associated with LBW and SGA.³⁶

Nonetheless, a few studies have reported contradictory associations.^{34,37} A study conducted in Turkey found a significant correlation between birth weight and an increase in maternal Hb from the first to the third trimester.³⁴ Another study from the United Kingdom found no significant association between changes in Hb levels during late pregnancy and low birth weight.³¹ The disagreement could be due to the inclusion of changes during the third trimester in the Turkish study, whereas our study focused only on the second trimester, when plasma volume expansion is typically at its peak, or the use of pre-pregnancy Hb levels as baseline in the United Kingdom, whereas our study used first-trimester Hb levels as baseline.

The mechanisms underlying the relationship between maternal Hb change and birth weight outcomes remain unclear. The typical increase in red blood cell mass as pregnancy advances into the second trimester is concurrent with a proportionately larger increase in plasma volume, resulting in a net decrease in maternal Hb concentration.^{1,36–38} Such an appreciable increase in plasma volume, and in turn, a decrease in maternal Hb levels, may be essential for maintaining normal fetoplacental circulation; its absence could potentially cause problems, including those related to fetal growth.^{38–40} The importance of appropriate Hb reduction during the course of pregnancy was long highlighted in a large (N=153,602), multi-ethnic cohort of pregnant women in the UK.⁴¹ In that study, Steer et al concluded that failure of maternal Hb to drop below 105 g/L was associated with an increased risk of adverse outcomes, including LBW.⁴¹

More recently, Burden et al hypothesized that the decline in maternal Hb concentration during mid-trimester may reflect optimal physiologic changes, indicating the body's ability for good plasma volume expansion.⁴² However, a lack of appropriate plasma expansion as pregnancy progresses may result from impaired placental function, leading to adverse outcomes and minimal decline in Hb concentration.⁴³ Smaller declines in Hb levels during the first trimester might indicate reduced or physiologically insufficient plasma volume expansion, which could impair fetoplacental circulation, affect fetal growth, and result in LBW and SGA babies.³⁹

Implication of the Findings

Our findings have important implications for the monitoring of changes in Hb concentration and, in turn, plasma expansion during antenatal care. They highlight the need to account for the physiological decline in Hb concentration due to plasma volume expansion when assessing anemia risks during pregnancy. A smaller decrease in Hb concentration during the second trimester may indicate inadequate plasma expansion, which is essential for optimal fetal growth. Monitoring changes in Hb concentration during the second trimester can help identify women at risk of insufficient plasma volume expansion and enable timely interventions, such as antenatal care and nutritional counseling, to prevent adverse outcomes, including low birth weight. Additionally, the overall decline in Hb concentration during the second trimester was 9 g/L, nearly double the commonly accepted threshold of 5 g/L.⁴⁴ Notably, women in the lowest-risk group for adverse birth weight outcomes experienced a median Hb decrease of 17 g/L. These findings suggest that the current threshold for Hb concentration decline in the second trimester may need to be re-evaluated. Future research is warranted to explore social determinants (nutrition, access to prenatal care, cultural practices) that may affect Hb changes. Moreover, future studies should elucidate the mechanisms underlying the relationship between maternal Hb changes and birth-weight-related outcomes.

Strengths and Limitations

A key strength of our study is that it is the first, and among a few globally, to examine birthweight-related adverse pregnancy outcomes in relation to changes in Hb levels in a large cohort of pregnant women. Most studies reporting on the association between maternal Hb and birthweight-related outcomes used a single Hb measurement rather than accounting for changes in Hb throughout pregnancy.^{13,19,25–28} Using a single Hb measurement can limit the ability to thoroughly analyze the pattern and impact of maternal Hb changes throughout pregnancy. Additionally, we were able to properly adjust the association for multiple variables, including early-pregnancy BMI,⁴⁵ that might confound the relationship between changes in maternal Hb and birth weight outcomes.

On the other hand, the interpretation of our findings may be limited, as the data are derived from women who attended antenatal care centers in one city. Hence, the generalizability of the findings to the rest of the UAE should be done with caution. Additionally, we could not adjust for placental conditions, such as placental insufficiency, which may influence the association between maternal Hb changes and birth-weight-related outcomes. Further adjustments for other socioeconomic, behavioral and clinical factors, for instance, smoking and iron supplementation before and during pregnancy, and hemoglobinopathies, should be adapted in future research to control for any potential confounding effects.

Conclusion

Pregnant women with low Hb changes between the first and second trimesters experienced increased risks of LBW and SGA. Mean Hb levels during the second trimester demonstrated an inverse relationship with birth weight and SGA. Monitoring fluctuations in maternal Hb during early- to mid-pregnancy can help pregnancies at risk of fetal growth restriction, instead of relying on a single measurement.

Generative Artificial Intelligence

We acknowledge the journal's Artificial Intelligence policy. Generative AI tools (eg, ChatGPT) were used only to assist with language editing, grammar refinement, and formatting of the manuscript text. No AI-generated data, analysis, or

references were created or modified using these tools. The authors have thoroughly reviewed all content for accuracy and originality and take full responsibility for the scientific integrity of the manuscript.

Data Sharing Statement

All relevant data are available within the manuscript. Additional requests could be submitted to the Mutaba'ah Study after ethical approval.

Ethics Approval and Informed Consent

The Mutaba'ah Study is approved by the UAE University Human Research Ethics Committee (ERH-2017-5512) and the Abu Dhabi Health Research and Technology Ethics Committee (DOH/CVDC/2022/72). Informed written consent was obtained from all participants prior to data collection.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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