

## Influence of Maternal Anemia on Placental Volume with Study of Uterine Artery Doppler

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### ABSTRACT

**Objectives:** To study the influence of maternal hematocrit(Ht) and hemoglobin (Hb) level on placental volume with study of uterine artery Doppler.

**Subjects and Methods:** In this prospective study 40 pregnant ( singleton pregnancy) cases were selected from the outpatient clinic of Alzahra university Hospital. They were divided into two groups the study group (20 cases) were anemic ( iron deficiency) and the control group ( 20 cases) were healthy. For each case two scans for the placenta and fetal growth were performed, the first at recruitment and the second 5 weeks later. Placenta volume was measured at each visit using three dimensional ultrasound. The maternal Hb and ( Ht) were measured in each visit.

**Results:** It revealed a non statistical significance between maternal hemoglobin, hematocrit and placental volume during the 1st visit and 2<sup>nd</sup> visit in anemic group compared to the control group. As regards Doppler study of the uterine artery in the present study it was noted that the pulsatility index and resistance index showed a non significant increase in the anemic group compared to the control group.

**Conclusion:** Maternal iron deficiency anemia can affect placental growth and development. Placental volume increased with mild anemia during the first trimester but has no significant effect on fetal growth. The use of 3D ultrasound is more accurate and efficient safe technique of great value in evaluating placental growth and volume. Also, the study of uterine artery blood flow during the mid second trimester showed a nonsignificant increase of RI and PI with maternal anemia. Further study are needed for the effect of anemia on fetal growth during preconceptional, first, second, third trimester and the outcome of pregnancy.

**Key words:** Maternal anemia, Placental Volume, Uterine Artery Doppler.

Humberto Azpurua *et al.*<sup>(6)</sup> studied the use of two-dimensional ultrasound (2DUS) for evaluation of placental volume, Placental location and shape. Three-dimensional ultrasonography is shown to be an appropriate, safe, non-invasive and accurate technique for evaluating the placental volume (PV) at the first trimester<sup>(7)</sup>.

Uterine artery Doppler ultrasound found to be a useful, non invasive method with which to assess indirectly from the earliest stages of pregnancy changes in the uteroplacental circulation.<sup>(8)</sup> When abnormal uterine artery Doppler velocimetry was accompanied with maternal anemia the risk of adverse pregnancy outcome was increased<sup>(9)</sup>

This work aimed to assess the influence of maternal hematocrit and hemoglobin percent on placental volume, crown rump length and uterine artery Doppler.

### Patients and Methods

### Introduction

Anemia is an important prevalent and preventable disease which may have considerable complications for mothers and fetuses. More than half of the women in the world experience anemia during pregnancy<sup>(1)</sup>. Anemia in pregnant may contribute to an increased nutritional insult to the fetus, by further contributing to fetal growth retardation<sup>(2)</sup>. Iron deficiency is the cause of more than 90-95% of anemia during pregnancy<sup>(3)</sup>. According to The World Health Organization<sup>(4)</sup> Iron deficiency anemia (IDA) is the most common cause of nutritional anemia.

Fetal growth and well-being depend on the functional and structural components of the placenta<sup>(5)</sup>. Anemia has a tremendous effect on the placenta. Maternal anemia increases the volume of the placenta. Fetal hypoxemia usually develops as a consequence of maternal anemia.

Data was statistically analyzed using SPSS (statistical package for social science) program version 13 for windows for all the analysis. p value < 0.05 was considered statistically significant:

Student t- test was done for normally distributed quantitative variables to measure mean and standard deviation and p-value < 0.05 was considered significant. Paired sample t- test was done for distributed quantitative variables to measure mean, standard deviation, correlation and p-value < 0.05 was considered significant.

### Results

In the present study, there was no statistical significant difference between the anemic and control groups as regards age, gravidity, parity, number of abortion, body mass index during first visit and second visit. The anemic group has a higher mean maternal age than the control group. The anemic group also had a lower BMI during 1st visit than the control group (Table 1).

Tables (2 & 3) showed that mean maternal hemoglobin and hematocrit during 1st visit in anemic group were (10.34 g/dl and 31.97 respectively) and were associated with non significant placental volume (79.29cm<sup>3</sup>) compared with that of the control group where the mean maternal hemoglobin and hematocrit were (12.42 g/dl and 37.5 respectively) and the placental volume was (69.11cm<sup>3</sup>).

Tables (4 & 5) showed that the low mean maternal hemoglobin and hematocrit in the anemic group were associated with non significant increased mean crown rump length in anemic group than in the control group which was (6.05 and 5.59 respectively).

Tables (6 & 7) showed that The anemic group had lower hemoglobin and hematocrit during the 2nd visit than in control groups (10.01, 31.3 and 11.51 and 35.34 respectively) and were associated with non significant placental volume than the control group which were (141.78 and 134.43) respectively.

Tables (8 & 9) showed that the anemic group has a lower mean maternal hemoglobin, and a non significant EFW (333.6Kg) during the 2nd visit compared with the control group EFW(326Kg).

Tables (10 & 11) revealed that the mean maternal hemoglobin and hematocrit were (10.01 mg/dl, 31.3) and (11.51 mg/dl, 35.34) in anemic and control group respectively and systolic diastolic ratio of uterine artery during the 2nd visit showed no difference between anemic and control groups. A non-significant statistical difference were found between maternal

This was a prospective study including forty pregnant women attending Al- zahraa university hospital outpatient clinic for routine hospital antenatal visit at 11- 14 weeks, during the period from June 2012 to June 2013.

Twenty cases were anemic pregnant (hemoglobin level was less than 11 gm/dl) The other Twenty were apparently healthy pregnant serving as a control (hemoglobin level more than 11 gm/dl), all cases were singleton pregnancy with living fetus at a gestational age between 11 and 14 weeks, of low risk pregnancy. Women with threatened miscarriage, multiple pregnancy, fetal anomalies or fetal death, Insulin-dependent diabetes, hypertension or heart disease were excluded. All individuals signed an informed consent. All the pregnant women were subjected to detailed history taking, complete clinical examination, Routine investigations including complete blood count (CBC), complete urine analysis, random blood sugar (RBS) kidney and liver function tests. Blood samples were taken at first visit at gestational age (11-14 weeks) to estimate hemoglobin and hematocrit levels using the Sysmex blood counter and assess their correlation with placental volume and crown rump length. Ultrasonographic examination: was performed using voluson 730 pro ultrasound machine (General Electric Medical System). Two dimensional ultrasonography was performed for all women included in the study during the first visit (11-14 weeks) to confirm viable singleton pregnancy and to confirm gestational age by measuring the fetal crown-rump length (CRL). All the participants were scheduled to have 3D scan of the placenta for measurement of placental volume, using the same ultrasound machine which was equipped with transabdominal volumetric probe its frequency ranged from 3.5 – 5 MHZ. Calculation of placental volume was made using the nomogram of Carla *et al.*<sup>(10)</sup> and Nowak *et al.*<sup>(11)</sup>. Women were requested to return for a second visit at 19 - 22 weeks for follow up. During this 2<sup>nd</sup> visit, color uterine artery Doppler velocimetry including S/D ratio (systolic/diastolic ratio), pulsatility index (PI) and the resistance index (RI) were calculated by the same examiner and by using the same machine. Another blood sample was taken to estimate hemoglobin and hematocrit levels to assess their correlation with placental volume and EFW.

### Statistical analysical

resistance index (RI) of uterine artery during the 2nd visit in both anemic and control groups.

Tables (14 & 15) revealed that the pulsatility index (PI) of uterine artery was higher in the anemic group (1.63) than that of the control group (1.27). Non-significant statistical difference were found between maternal hemoglobin (Hb), hematocrit and pulsatility index (PI) of uterine artery during the 2nd visit in both anemic and control groups. P value > 0.05

hemoglobin (Hb), hematocrit (HCT) and systolic diastolic ratio (SD ratio) of uterine artery during the 2nd visit in both anemic and control groups

Tables (12 & 13) revealed that the resistance index (RI) of uterine artery was higher in anemic group (0.77) than that of the control group (0.56). A non-significant statistical difference were found between maternal hemoglobin (Hb), hematocrit (HCT) and

**Table (1): The demographic data of both anemic and control groups.**

	<b>Group I (Anemic) N=20, mean± SD</b>	<b>Group II (Control) N= 20, Mean± SD</b>	<b>t.test</b>	<b>P.value</b>
<b>Age(year)</b>	28.3±4.5	26.7±5.2	1.072	NS
<b>Gravidity</b>	3.4±1.6	2.8±1.6	1.218	NS
<b>Parity</b>	1.9±0.9	1.8±1.1	0.268	NS
<b>Abortion</b>	0.7±1.0	0.3±0.6	1.437	NS
<b>Height(cm)</b>	160.75±6.03	160.8±6.57	-0.06	NS
<b>Weight 1<sup>st</sup>(kg)</b>	71.67±13.06	73.2±14.4	-0.36	NS
<b>Weight 2<sup>n</sup>(kg)<sup>d</sup></b>	72.6±13.8	74.8±14.2	-0.52	NS
<b>M BMI 1<sup>st</sup>(Kg/m<sup>2</sup>)</b>	27.90±5.7	28.34±5.34	-0.25	NS
<b>BMI 2<sup>nd</sup>(Kg/m<sup>2</sup>)</b>	28.42±5.98	28.96±5.25	-0.3	NS

P. value > 0.05 is non significant P. value < 0.05 is significant

**Table (2): The correlation between maternal hemoglobin (Hb), and placental volume (pv) during the 1st visit in both anemic and control groups.**

	Hb first visit	Pv first visit	Correlation*	P
Anemic	10.34±0.56	79.29±17.44	-0.31	0.19
Control	12.42±1.03	69.11±18.45	0.00	1.00

\*Paired sample test

**Table (3) : The correlation between maternal hematocrit (HCT) and (pv) during the 1st visit in both anemic and control groups.**

	HCT first visit	Pv first visit	Correlation*	P
Anemic	31.97±1.63	79.29±17.44	-.186	.432
Control	37.50±3.43	69.11±18.45	0.11	0.65

\*Paired sample test

**Table (4): The correlation between maternal (Hb) and crown rump length (CRL) during the 1st visit in both anemic and control groups.**

	Hb first visit	CRL first visit	Correlation*	P
Anemic	10.34±0.56	6.05±1.38	-.305	.191
Control	12.42±1.03	5.59±1.41	0.13	0.59

**Table (5): The correlation between (HCT) and (CRL) during the 1st visit in both anemic and control groups.**

	HCT first visit	CRL first visit	Correlation*	P
Anemic	31.97±1.63	6.05±1.38	-.426	.061
Control	37.50±3.43	5.59±1.41	0.03	0.90

**Table (6): The correlation between (HCT) and (pv) during the 2nd visit in both anemic and control groups.**

	HCT second visit	Pv second visit	Correlation*	P
Anemic	31.30±2.61	141.78±35.25	-.316	.175
Control	35.34±2.79	134.43±25.56	-0.09	0.70

**Table (7): The correlation between maternal (Hb) and (pv) during the 2nd visit in both anemic and control groups.**

	Hb second visit	Pv second visit	Correlation*	P
Anemic	10.01±0.89	141.78±35.25	-.250	.288
Control	11.51±1.10	134.43±25.56	-0.14	0.56

**Table (8): The correlation between maternal (Hb) and estimated fetal weight (EFW) during the 2nd visit in both anemic and control groups.**

	Hb second visit	EFW second visit	Correlation*	P
Anemic	10.01±0.89	333.60±104.08	-.333	.152
Control	11.51±1.10	326±85.71	-0.09	0.70

**Table (9): the correlation between maternal hematocrit and estimated fetal weight (EFW) during the 2nd visit in both anemic and control groups.**

	EFW second visit	HCT second visit	Correlation*	P
Anemic	333.60±104.08	31.3±2.6	-12.88	0.00
Control	326±85.71	35.34±2.79	-15.1	0.00

**Table (10): The correlation between maternal (Hb) and systolic diastolic ratio (SD ratio) of uterine artery during the 2nd visit in both anemic and control groups.**

	Hb second visit	SD second visit	Correlation*	P
Anemic	10.01±0.89	5.34±7.24	-.091	.704
Control	11.51±1.10	5.34±7.24	-0.14	0.55

**Table (11): The correlation between maternal (HCT) and (SD ratio) of uterine artery during the 2nd visit in both anemic and control groups.**

	HCT second visit	SD second visit	Correlation*	P
Anemic	31.30±2.61	5.34±7.24	-.110	.644
Control	35.34±2.79	4.10±4.25	-0.21	0.38

**Table (12): The correlation between maternal (Hb) and resistance index (RI) of uterine artery during the 2nd visit in both anemic and control groups.**

	Hb second visit	RI second visit	Correlation*	P
Anemic	10.01±0.89	0.77±0.49	-.034	.887
Control	11.51±1.10	0.56±0.27	-0.22	0.36

**Table (13): The correlation between maternal (HCT) and (RI) of uterine artery during the 2nd visit in both anemic and control groups.**

	HCT second visit	RI second visit	Correlation*	p
Anemic	31.30±2.61	0.77±0.49	-.176	.458
Control	35.34±2.79	0.56±0.27	-0.09	0.71

**Table (14): The correlation between maternal (Hb) and pulsatility index (PI) of uterine artery during the 2nd visit in both anemic and control groups.**

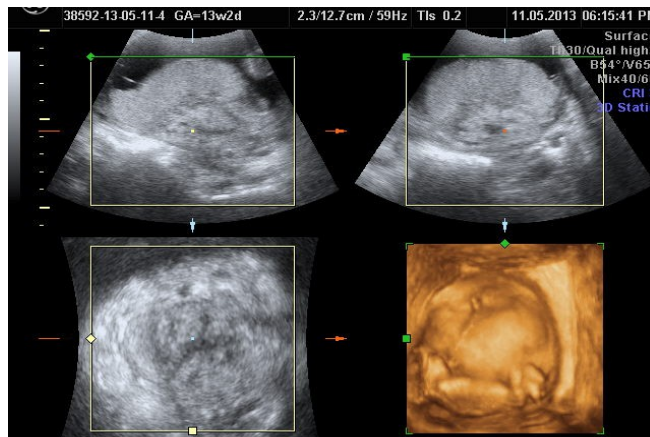
	Hb second visit	PI second visit	Correlation*	P
Anemic	10.01±0.89	1.63±1.02	-.125	.600
Control	11.51±1.10	1.27±0.81	-0.23	0.32

**Table (15): The correlation between maternal (HCT) and (PI) of uterine artery during the 2nd visit in both anemic and control groups.**

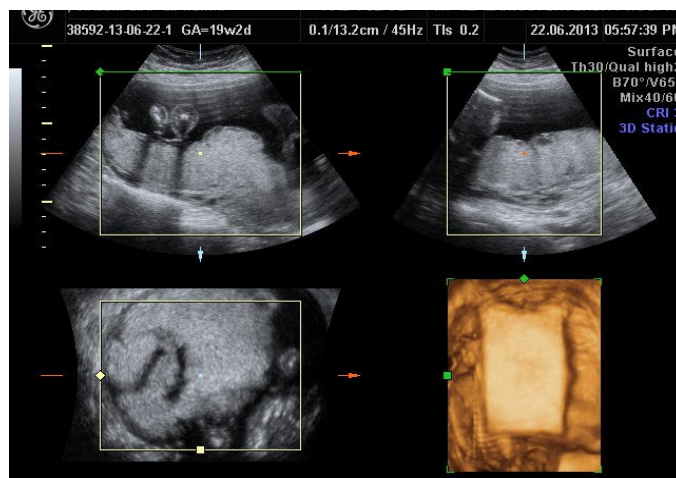
	HCT second visit	PI second visit	Correlation*	P
Anemic	31.30±2.61	1.63±1.02	-.234	.321
Control	35.34±2.79	1.27±0.81	-0.21	0.38

**Fig. (1) : (Anemic case)**

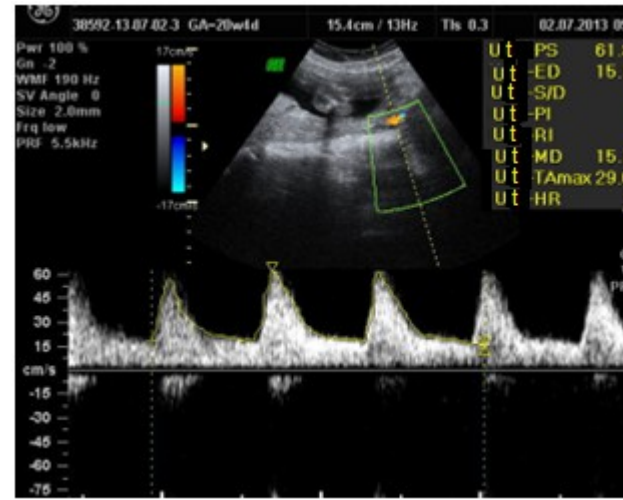
**Fig. (1-a): Measurement of placental volume at 13 week gestation (First visit)**



**Fig. (1-b): Measurement of placental volume at 19 week gestation (Second visit)**

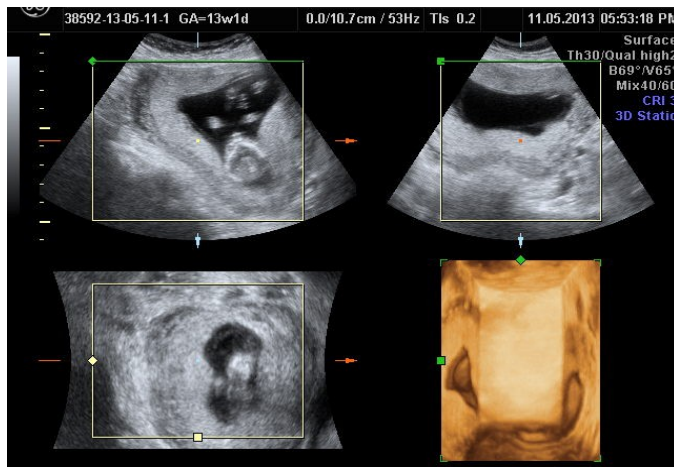


**Fig. (1-c) : Uterine artery Doppler indices at 19 week gestation (second visit)**

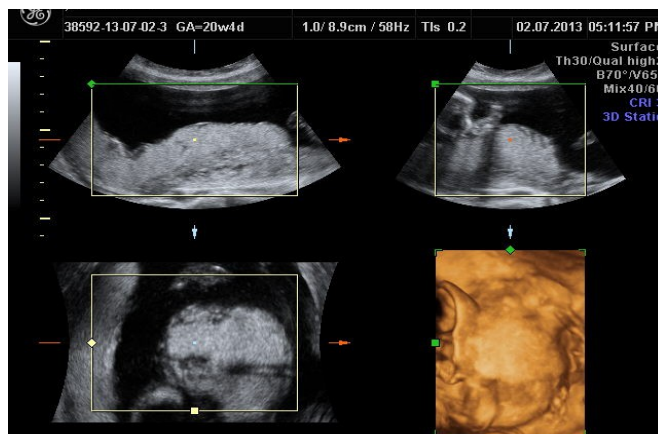


**Fig. (2) : control case**

**Fig. (2-a) : Measurement of placental volume at 13 week gestation (First visit)**

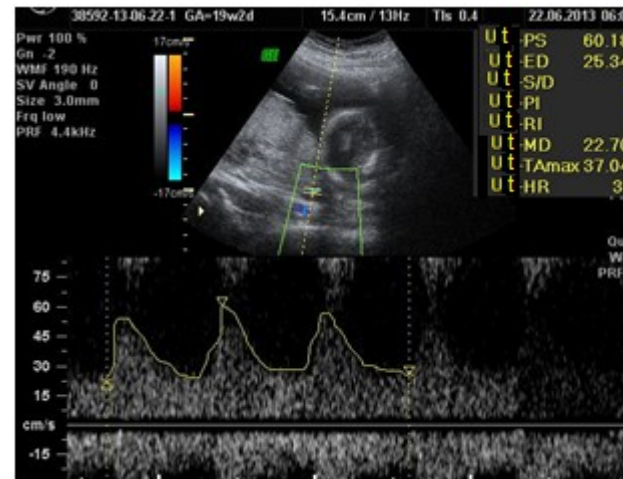


**Fig. (2-b): Measurement of placental volume at 20 week gestation (Second visit)**





**Fig. (2-c): Uterine artery Doppler indices at 20 week gestation (second visit)**



increases fetal cortisol production, and cortisol may inhibit longitudinal growth of the fetus. An alternative mechanism could be that iron deficiency increases oxidative damage to erythrocytes and the fetoplacental unit<sup>25</sup>.

Women with severe anemia at all stages of pregnancy doubled the risk of delivering LBW infants; when stratifying according to trimester of pregnancy, the association was found to be stronger for severe anemia in the first trimester with a 15-fold increase in the risk. Results from a study in India also suggested a negative effect of anemia during pregnancy on different anthropometric measurements at birth. Contrary to these results, two studies in different populations (United States and United Kingdom) did not find a relationship between iron status markers (hemoglobin or mean corpuscular volume [MCV]) at different stages of pregnancy and fetal growth outcomes. It is important to consider that in the British study only 3% of the sample had hemoglobin levels under 11 g/dL at 12 weeks.

Milan Stefanović *et al*.<sup>26</sup> found that only severe anemia (maternal hemoglobin < 60 g/l) triggered fetal cerebral vasodilatation, however the uterine index was normal in this group and also in the group whose hemoglobin was > 60g/l.

Absence of fetal blood flow redistribution for maternal hemoglobin level of >60 g/l suggests that the oxygenation of the fetus was still satisfactory this may be due to the huge placental reservoir of maternal blood; therefore, even if the maternal blood oxygen content is lower than normal, there is enough oxygen passing through the placenta.<sup>27</sup>

We can conclude that anemia can affect placental growth and development. Placental volume may be increased with maternal anemia. The use of 3D ultrasound is a safe technique of great value in evaluating placental growth and volume. It is more accurate and efficient than 2D ultrasound in measurement of placental volume. The use of Doppler ultrasound is an efficient method for evaluation of uteroplacental circulation. Uterine artery blood flow increase with maternal anemia.

We may recommend to prevent and treat anemia, as it can affect both mother and fetus, also it can affect placental growth and development.

Use of 3DUS is of great value than 2DUS in measurement of placental volume as it is safe and more accurate technique. Also Doppler ultrasound is recommended for uterine artery blood flow

significant for neonatal weight, length and head circumference.

During the 2nd visit in the present study, there was a non statistical significance between maternal hemoglobin (Hb), hematocrit (HCT) and placental volume (pv).

The present study shows that maternal hemoglobin during the second visit has a non statistical significance with estimated fetal weight in the anemic group and in the control group.

Effect of maternal anemia on intrauterine growth is attributed to chronic deprivation of oxygen to the developing fetus. Severe maternal anemia if present from early gestation may be associated with reduced placental weight and structural abnormalities of the placenta<sup>22</sup>, which in turn affect nutrient transport from the mother to the fetus, this explains how maternal anemia adversely affects fetal growth<sup>23</sup>

Malhotra *et al*.<sup>24</sup> found that the biggest newborn birth weight was denoted among women with hemoglobin concentration ranging between 9.6 and 10.5 gm/dl.

Nardoza *et al*.<sup>7</sup> classified anemia as mild if hemoglobin was 10-10.9(g/dL), moderate (7.0-9.9), severe (<7.0) and very severe (decompensated) (<4.0). This might explain why in the present study there was no significant difference between the study and the control group as regards fetal crown rump length and EFW.

As regards Doppler study of the uterine artery in the present study it was noted that the pulsatility index and S/D ratio and resistance index showed a non statistical significance with maternal hemoglobin and hematocrit during the second visit in both anemic and control groups although there was an increase in the RI, and PI index and S/D ratio in the anemic group.

This could be explained by the persistence of low Hg and HCT (mild anemia) during the second trimester might lead to changes in placental vasculature to adapt for the decrease in oxygen supply

Several potential biological mechanisms have been proposed by Rolo *et al*.<sup>25</sup> to explain the pathways through which iron deficiency, including its more severe form, anemia, could impair fetal growth.

Anemia (by causing hypoxia) and iron deficiency (by increasing serum norepinephrine concentrations) can induce maternal and fetal stress, which stimulates the synthesis of corticotropin-releasing hormone (CRH). CRH also



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