

The Relationship of Uterine Artery Doppler Velocimetry Findings and Hemoglobin Concentration with Pregnancy Outcomes in Pre-eclampsia

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Abstract

Background: Epidemiologic studies have shown the relationship of maternal hemoglobin level and abnormal findings in uterine Doppler sonography with pregnancy-related complications. In this study, we evaluated the relationship of uterine artery Doppler velocimetry findings and hemoglobin level with the outcomes of pregnancy in women with preeclampsia and healthy women.

Methods: In this prospective study performed from September 2013 to September 2014, 50 patients with Preeclampsia in the third trimester (more than 28 weeks) referred to Afzalipour Hospital, Kerman/Iran and 50 healthy pregnant women who attended the perinatology clinic for prenatal care, were randomly selected. The results of uterine artery Doppler, hemoglobin concentration and outcome of pregnancy were compared between the two groups.

Results: Twenty nine patients (51%) with preeclampsia and 17 patients (34%) in the control group had abnormal Doppler findings. In both groups, birth weight was lower in women with abnormal Doppler findings compared to the women who had normal sonography findings ($p=0.024$ and $p=0.008$, respectively); furthermore, in both groups, gestational age at birth time was lower in women with abnormal sonography findings ($p=0.044$ and $p=0.012$, respectively). The average hemoglobin concentration was not statistically different between the two groups and abnormal Doppler findings showed no significant relationship with the mean concentration of hemoglobin in none of the two groups.

Conclusion: This study showed that abnormal findings in Doppler of the uterine artery are associated with adverse pregnancy outcomes such as low birth weight and premature births and the coexistence of preeclampsia is associated with worse pregnancy outcomes.

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Introduction

Preeclampsia is a major cause of mortality and morbidity in both mother and fetus, affecting 2-10% of all pregnancies (1, 2).

Improper invasion of the trophoblastic cells to the spiral arteries causes low placental perfusion and eventually leads to

the increased uterine artery resistance. Increase in the uterine artery flow rate is determined by Doppler ultrasound, which is an indirect indicator of this phenomenon. Histological studies have shown that abnormal invasion to the spiral arteries is associated with fetal growth restrictions and preeclampsia (3). Abnormal Doppler finding of uterine artery could be used to screen high-risk women in need of fetal and maternal

surveillance. Reports exploring the value of reassessment of uterine artery Doppler in the third trimester of pregnancy have concluded that persistence of increased uterine artery resistance is associated with an increased risk of obstetric complications (4, 5).

Hemoglobin level slightly decreases during pregnancy due to relatively greater increase of the plasma volume in comparison to the increase of red blood cells. Some studies have shown that patients with anemia are at higher risks of preterm delivery and low birth weight (6).

Epidemiologic studies have shown the relationship between maternal hemoglobin concentration and increased risk of complications in pregnancy. The pathophysiology of this condition during pregnancy could be attributed to the fact that high concentration of hemoglobin decreases plasma volume and consequently the fetal placental perfusion resulting in fetal distress (7, 8).

Since hemoglobin concentration on both sides of the spectrum and increased resistance of the uterine arteries are both associated with adverse outcomes in pregnancy and considering that few studies have evaluated these factors together, in this study we evaluated the relationship of hemoglobin concentration and the findings of the uterine artery Doppler sonography with adverse pregnancy outcomes in women with preeclampsia.

Materials and methods

In this prospective study performed from September 2013 to September 2014, 50 pregnant women in the third trimester (more than 28 weeks) with Preeclampsia referred to Afzalipour Hospital, Kerman/ Iran were considered as the case group and 50 healthy pregnant women attended the perinatology clinic for prenatal care, were randomly selected as the control group. All patients gave their written and informed consent to enter the study (2). The study protocol was approved by the Ethics Committee and the Institutional

Review Board of Kerman University of Medical Sciences (k/92/422).

Women with multiple pregnancy, history of chronic hypertension, diabetes mellitus, autoimmune diseases, drug abuse and fetal anomalies were excluded.

Study data were retrieved through interviewing patients and their companions. The collected data included age, gravidity, date of last menstrual period, medical history and details of symptoms such as headache, visual disturbance, epigastric pain, edema, oliguria or convulsions. Laboratory examinations were undertaken including complete blood count and liver and kidney function tests.

Uterine artery Doppler velocimetry was performed with the medisonAccuvix 10 ultrasound scanner at the crossover of the uterine and external iliac arteries with an insonation angle of less than 30, a velocity of more than 60cm/s and a sample volume of 2.0mm. Both sides were measured three times and mean of results was recorded. Doppler examination was performed by a perinatologist. Uterine artery RI (Resistance Index) and PI (pulsatility Index) of >95th percentile from standard values and presence of early diastolic notch were classified as abnormal (9).

Mild preeclampsia was considered as a blood pressure of 140/90 and higher, measured at least 2 times, 6 hours apart with proteinuria of +1 on dipstick or more than 300mg in the 24- hour urine sample in women with gestational age of more than 20 weeks. Severe preeclampsia was defined as blood pressure of more than 160/110 with proteinuria of 2 grams in the 24- hour urine sample or more than +1 on dipstick or one that is associated with multi-organ involvement including pulmonary edema, convulsions, oliguria (less than 500cc of urine in 24 hours), thrombocytopenia (platelet count less than 100,000), abnormal liver enzymes with continuous epigastric or right upper quadrant pain or the presence of persistent neurological symptoms (headache, blurred vision, blindness, altered level of consciousness).

These patients were followed up until delivery, and details of pregnancy events, labor and delivery, and neonatal outcome were noted.

Data were analyzed using the Statistical Package for Social Sciences software, SPSS for windows, version 16 (SPSS Inc., Chicago, IL, USA). For comparison of quantitative data between the two groups, independent t-test and for comparison of qualitative data, Chi-square test was used. All data are displayed as mean \pm standard deviations and frequency and percent. A two-tailed p-value of less than 0.05 was considered as statistically meaningful.

Results

A total of 50 pregnant women with preeclampsia (study group) and 50 women with normal pregnancy (control group) were evaluated.

Among women with preeclampsia, 21 patients (49%) had normal findings in Doppler of the uterine artery and 29 patients (51%) had abnormal findings. In the control group, there were 33 patients (66%) with normal Doppler uterine artery and 17 patients (34 %) had abnormal Doppler findings.

In the case group, among women who had normal Doppler findings, 4 (19%) patients had severe preeclampsia, 8 (38/1%) patients had mild preeclampsia and 9 (42/9%) patients had mild preeclampsia that became severe during the course of pregnancy. Among those with abnormal Doppler findings in the case group, 14 (48/3%) patients had severe preeclampsia, 7 (24/1%) patients had mild preeclampsia and 8 (27/6%) patients had mild preeclampsia that became severe during the course of pregnancy. This difference between these two groups was not statistically significant ($P = 0.105$).

In the case group, mean maternal age and gravidity was not different between the groups with normal and abnormal Doppler findings. Although mean hemoglobin concentration

was higher in those with abnormal Doppler findings than those with normal Doppler findings, the difference was not statistically significant ($P = 0.351$). In women with preeclampsia, mean gestational age at time of delivery in the group with abnormal Doppler findings was lower compared to those with normal Doppler findings (34.1 ± 3.06 weeks vs. 36.1 ± 2.35 weeks, $p = 0.012$). In the case group, birth weight was lower in women with abnormal Doppler than in those with normal Doppler findings ($p = 0.008$).

In the control group, mean gestational age at time of delivery was lower in women with abnormal Doppler findings than those with normal Doppler findings ($p = 0.044$). In this group, birth weight was also lower in those with abnormal Doppler findings compared to those with normal Doppler findings (3040.30 ± 370.59 gr vs. 3278.82 ± 283.17 gr, $p = 0.024$). Mean concentration of hemoglobin in the control group was not different between those with normal and abnormal Doppler findings. Comparison of the case and control groups showed that among those patients with abnormal Doppler findings, mean concentration of hemoglobin in patients with preeclampsia was higher, although this difference was not statistically significant ($p = 0.496$). In patients with abnormal Doppler findings, birth weight was lower in women with preeclampsia compared to women with normal blood pressure ($p < 0.001$). Also, the gestational age at time of delivery was lower in women with abnormal Doppler findings who were in the case group rather than in the control group ($p < 0/001$). The results have been shown in table 1.

No relationship was found between the results of Doppler sonography and hemoglobin concentration in the two groups. The relationship of hemoglobin concentration with preterm labor and SGA can be seen in table 2).

Table 1. Comparison of pregnancy- related outcomes between case and control groups based on the sonography findings

Variables	Abnormal sonography (n=46)			Normal sonography (n=54)		
	Case (n=29)	Control (n=17)	p-value	Case (n=21)	Control (n=33)	p-value
Maternal age (yrs)	28 ± 4.97	27 ± 6.93	0.573	28.1 ± 3.79	26.6 ± 3.88	0.177
Gravidity (no.)	1.62 ± 0.72	1.41 ± 0.5	0.303	1.52 ± 0.16	1.63 ± 0.14	0.625
Hemoglobin (mg/dl)	13.53 ± 3.53	13.34 ± 1.12	0.831	12.78 ± 1.01	13.06 ± 1.13	0.346
GA at birth(wks)	34.1 ± 3.06	38.53 ± 0.68	<0.001	36.10 ± 2.35	38.01 ± 0.9	<0.001
Birth weight (gr)	2032.58 ± 818	3278.82 ± 283.1	<0.001	2610.95 ± 144.9	3040.3 ± 64.51	0.004
SGA [no. (%)]	11 (85)	2 (15)	<0.001	2 (50)	2 (50)	0.636

* All plus-minus values are means ± standard deviations unless stated otherwise. Some of the values have been rounded for better evaluation; the case group represents preeclampsia patients and the control group consists of normal pregnant patients.

Table 2. Pregnancy related outcomes and their relationship with hemoglobin concentration

Variables	Case group (n=50)			Control group (n=50)	
	Hemoglobin concentration	Correlation coefficient (r)	p-value	Correlation coefficient (r)	p-value
Gravidity (no.)		-0.04	0.783	-0.24	0.092
GA at birth (wks)		-0.16	0.251	0.501	<0.001
Maternal age (yrs)		-0.19	0.165	0.292	0.04
Birth weight	Normal	12.85 ± 1.06	0.359		
	SGR	14.23 ± 14.95			
Preeclampsia severity	Mild	12.86 ± 1.19	0.529		
	Moderate	13.84 ± 4.54			
	Severe	12.92 ± 0.99			

* All plus-minus values are means ± standard deviations unless stated otherwise.

Discussion

Doppler ultrasound can be used to evaluate the utero-placental and embryonic blood flow and to predict the maternal and fetal outcomes. Resistance of the uterine artery is evaluated using Doppler related indexes such as systole/diastole ratio, resistance index and the pulse index. Use of Doppler uterine artery for predicting pregnancy outcomes in preeclampsia and IUGR has been proposed for gestational ages of 11-14 weeks and 20-23 weeks, in the past decade (10-13).

One study in 2005 investigated the relationship between uterine vascular resistance and impairment of trophoblast cell invasion in patients with preeclampsia. In the mentioned study, 32 pregnant women with preeclampsia (12 with mild and 20 with severe preeclampsia) and 20 healthy pregnant women were chosen as the case and control group, respectively. It was found that trophoblast cell invasion into the spiral arteries had occurred in 75% of the women with mild preeclampsia, 55% of the women with severe preeclampsia and in 100% of the normal women. Similar to our results, in the mentioned study, the difference between the mild and severe preeclampsia groups was not statistically significant ($p > 0.05$), but the difference between the preeclampsia and normal groups was significant (14).

In low risk pregnancy, the association of the existence of a unilateral or bilateral notch in the 24-26th gestational weeks with preeclampsia and IUGR is under debate. In high-risk pregnant women, the existence of a unilateral or bilateral notch after 24 weeks is 60% associated with adverse pregnancy outcomes. In a study by Hunkapiller et al, Doppler of the uterine artery was studied in women with preeclampsia. They found an association between the existence of notches and adverse pregnancy-related outcomes (15).

Few studies have investigated the value of Doppler of the uterine artery in predicting pregnancy outcomes in the third trimester. In our study, the relationship between low birth

weight and preterm delivery with abnormal findings in uterine Doppler was significant in both groups. Comparison of those with abnormal Doppler uterine arteries in the two groups showed that pregnant women with preeclampsia and abnormal Doppler findings had lower birth weights and lower gestational ages in time of birth.

In a case-control study conducted in Italy in 2002, 106 women with abnormal findings in uterine Doppler and 186 women with normal findings in their 34th week of pregnancy were studied. According to the results, increase in the placental vascular resistance and impaired Doppler uterine artery did not show a relationship with maternal age, maternal BMI, preeclampsia, transmission of the baby to NICU, intrauterine death and maternal complications ($p < 0.001$) but it had a meaningful relationship with reduction in birth weight (16). Overall, our findings are similar to the results of the mentioned study.

In our study there was no relationship between mean hemoglobin concentration and Doppler of the uterine artery; furthermore, hemoglobin concentration did not have a meaningful relationship with premature birth and SGA in the two groups. However, studies have shown that hemoglobin concentration is associated with the risk of premature birth, fetal death and preeclampsia (17). In an earlier study in 2007, the significance of Doppler ultrasound as a predictor of adverse outcomes was studied in women with anemia in the third trimester of pregnancy. It was concluded that anemia in women with abnormal findings in uterine Doppler sonography is associated with increase in the risk of some adverse pregnancy-related events including fetal distress, premature birth and low birth weight (6). In one study in 2014, the relationship between the parameters of iron with preeclampsia was evaluated and it was found that serum iron and ferritin levels were significantly higher in women with preeclampsia than normal women. However, similar to our

study, hemoglobin concentration in the two groups had no significant difference ($p < 0.001$).

Makuyan et al. (18) and Hershkowitz et al. (19) reported similar findings to our study and found no significant difference between the two groups of preeclampsia and normal pregnancy in regard to the concentrations of hematocrit and hemoglobin. However, according to some reports, CBC parameters are higher in women with preeclampsia (20).

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