

Effect of placental laterality on uterine artery resistance and development of preeclampsia and intrauterine growth retardation

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We studied 153 pregnant women with normal pregnancies and 147 women with complicated pregnancies (diabetes, hypertensive disorders, and intrauterine growth retardation) to evaluate the association of placental location and the development of preeclampsia, intrauterine growth retardation, and uterine artery resistance. The placental location was determined by real-time ultrasonography, and the uterine artery resistance was determined by continuous-wave Doppler flow velocity waveform analysis. In the presence of preeclampsia or intrauterine growth retardation, up to 75% of the patients had unilaterally located placentas and 25% central placentas, whereas in the absence of these two conditions only 51% of the patients had unilateral and 49% central placentas ($p < 0.02$). In patients with unilateral placentas, the incidence of preeclampsia and intrauterine growth retardation was 2.8-fold and 2.7-fold greater than in patients with central placentas ($p < 0.03$ and $p < 0.01$). Among all patients unilateral placental location was more likely to be associated with abnormal uterine artery flow velocity waveforms than central placental location ($p < 0.001$). We conclude that unilateral placental location may predispose to the development of preeclampsia and intrauterine growth retardation by its effect on uterine artery resistance. (AM J OBSTET GYNECOL 1989;161:1536-9.)

Key words: Placenta, preeclampsia, intrauterine growth retardation, flow velocity waveform analysis

The significance of placental location in the uterine cavity has been studied extensively. Placental location has been found to correlate with fetal position and presentation,^{1,2} length of gestation,³ course of labor,⁴ presence of preeclampsia,^{5,6} and pregnancy outcome.⁷ Several methods have been used to document placental location, including manual exploration of the uterus, soft tissue x-ray films, and isotopic placentography.^{1,8-11} In the past two decades ultrasonography has proved to be the safest, easiest, and most accurate method for assessing placental location.^{2,12,13}

The relationship between placental location and the development of preeclampsia has been examined previously with controversial results.^{5,6} In the two previous reports the placental location was examined with regard to its proximity to the uterine fundus. The two groups used different methods. There has been no study to examine the clinical significance of placental laterality and its association with the development

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Table I. Patient characteristics according to placental location

	Placenta location		p Value
	Central	Unilateral	
Maternal age (mean \pm SD)	23.9 \pm 6.0	23.9 \pm 5.3	1.00
Gravidity (mean \pm SD)	2.0 \pm 1.1	1.9 \pm 1.2	0.92
Parity (mean \pm SD)	0.6 \pm 0.8	0.6 \pm 0.8	0.84

of preeclampsia and intrauterine growth retardation (IUGR). There is a significant association between placental location and uterine artery resistance.¹⁴ It is possible that placental location may influence uterine artery blood flow distribution and predispose the pregnancy to such adverse outcomes as preeclampsia, premature birth, and IUGR. This study was designed to examine the association of placental laterality and uterine artery resistance and the development of preeclampsia and IUGR.

Material and methods

A total of 311 patients were enrolled in the study. Eleven were excluded because of insufficient pregnancy outcome information. Of the remaining 300 patients, 153 had normal uncomplicated pregnancies, and 147 patients had pregnancies complicated by diabetes

Table II. Relationship of placental laterality and presence or absence of preeclampsia, IUGR, or both

Placental location	Preeclampsia		IUGR		Preeclampsia, IUGR, or both		
	Yes	No	Yes	No	Yes	No	
Central	9 (26%)	129 (49%)	11 (25%)	127 (49%)	16 (28%)	117 (48%)	
Unilateral	25 (74%)	137 (51%)	30 (75%)	132 (51%)	41 (72%)	126 (52%)	
χ^2 test		$p < 0.03$		$p < 0.02$		$p < 0.007$	

Table III. Incidence of preeclampsia and IUGR in study group according to placental location

Placental location	Presence of preeclampsia		Presence of IUGR	
	Yes	No	Yes	No
Central	9 (6.5%)	129 (93.5%)	11 (8%)	127 (92%)
Unilateral	25 (15.4%)	137 (84.6%)	30 (18.5%)	132 (81.5%)
$\chi^2, p > 0.08$		$\chi^2, p > 0.01$		

mellitus ($n = 39$), hypertensive disorders ($n = 69$), and pregnancies suspected of IUGR ($n = 39$). Of the 39 women with diabetes 18 had gestational diabetes and 21 had insulin-dependent diabetes. The normal patients were recruited from a population referred to the ultrasonography unit for pregnancy dating and from the low-risk prenatal clinic. The high-risk patients were recruited from a population referred to the antenatal testing unit for fetal surveillance. All high-risk patients were examined during the third trimester of pregnancy. The majority of the normal patients were also examined during the third trimester, and the remainder were examined between 24 and 28 weeks of gestation. The study was approved by the institution's Clinical Research Practices Committee; all patients gave written informed consent.

Diagnosis and classification of the hypertensive disorders were according to criteria of the American College of Obstetricians and Gynecologists.¹⁵ Growth charts appropriate for our population were used to classify the infants as small for gestational age or appropriate for gestational age.¹⁶

The placental location was determined by real-time ultrasonography. The method has been previously described.¹⁴ In brief, the placenta was classified as right, left, or central regardless of its anteroposterior and fundal position. For the purpose of analysis the patients with right or left placentas were classified as having unilaterally located placentas. Placental location was evaluated without prior knowledge of the flow velocity waveforms. The interobserver variation in assignment of placental location was 13%.

The flow velocity waveforms were obtained with the mother lying comfortably in a slight left lateral tilt according to method that has been described previously.¹⁴ A 4 MHz continuous-wave Doppler device equipped with a real-time spectrum analyzer was used to obtain the uterine artery flow velocity waveforms. Briefly, two measurements were obtained from each side. The average of the two measurements on each side is classified as right uterine artery flow velocity waveform and left uterine artery flow velocity waveform, respectively. When necessary for comparisons, the mean of the right and left uterine arteries is classified as the uterine artery flow velocity waveforms. The uterine artery flow velocity waveforms were classified as abnormal if they

exceeded the 95th percentile of our normal values (systemic/diastolic ratio > 2.8 after 24 weeks' gestation). The intrabserver coefficient of variation for the flow velocity waveforms was 8%. Statistical significance of the results was evaluated by the χ^2 test. A value of $p < 0.05$ was considered statistically significant.

Results

Data from a total of 300 patients were used for analysis. There was no difference in the incidence of laterality between pregnancies < 28 weeks' gestation and those of > 28 weeks or between white and nonwhite patients. Maternal characteristics are listed in Table I. The incidence of the different placental locations with regard to laterality in the entire group was as follows: central, 46%; right-sided, 33%; left-sided, 21%. Thus the incidence of unilateral placenta was 54%. The group was not statistically different from the group of high-risk patients (52% vs. 56%). However, when the patients with preeclampsia and/or IUGR were grouped together and compared with the rest of the patients, significant associations and differences were found (Table II).

Patients with unilateral placental location had a 2.8-fold higher increase in the incidence of preeclampsia than patients with centrally located placentas ($p < 0.03$). Similarly, patients with unilateral placental location had a 2.7-fold increase in the incidence of IUGR than patients with centrally located placentas ($p < 0.01$, Table III).

Table IV. Placental laterality according to uterine artery flow velocity wave forms

Placental location	Right or left uterine artery		Mean of both sides	
	Abnormal	Normal	Abnormal	Normal
Central	20 (27%)	118 (52%)	16 (30%)	122 (49%)
Unilateral	55 (73%)	107 (48%)	37 (70%)	125 (51%)
χ^2 test	$p < 0.001$		$p < 0.02$	

Regardless of which vessel was examined (right or left uterine artery or the mean of the two sides), 70% to 73% of patients with abnormal flow velocity waveforms had unilaterally located placentas (Table IV). In the presence of preeclampsia and abnormal uterine artery flow velocity waveforms ($n = 20$), 16 (80%) of the patients had unilateral placentas and only four (20%) had centrally located placentas. In the presence of IUGR with abnormal uterine artery flow velocity waveforms ($n = 18$), 15 (83%) of the patients had unilateral placentas and only three (17%) had central placentas. In the group of diabetic patients five (13%) developed preeclampsia; four of those five patients (80%) had unilateral placentas and only one (20%) had a central placenta.

Comment

This study provides evidence of the existence of a significant association between placental laterality and the presence of preeclampsia, IUGR, or both. It also appears that the placenta is located laterally in the majority of patients with abnormal uterine artery flow velocity waveforms.

The association of placental location and the development of preeclampsia has been examined twice with contradictory results.^{5,6} Both reports examined the placental location with regard to the proximity of the placenta to the fundus. Booth et al.⁵ found a significant association between fundal placentas and the presence of preeclampsia; they explained it by Bieniarz's theory. Bieniarz¹⁷ theorized that when the placenta is located high in the uterine cavity, the draining of the uteroplacental circulation might cause a pathologic redistribution of blood in the renal and visceral circulation, resulting in preeclamptic toxemia. In contrast, Little and Friedman⁶ failed to find any association between highly implanted placentas and preeclampsia.

Preeclampsia and IUGR are both conditions strongly related to poor placental development and function. Khong et al.¹⁸ showed that poor trophoblastic conversion of the spiral arterioles leads to development of preeclampsia, IUGR, or both conditions. It has been shown in humans that both uterine arteries have a significant number of branches and that each supplies the corresponding uterine side. In some patients arcuate branches of the uterine artery cross over to the other

side and create major anastomoses.¹⁹ Although anatomic anastomoses between the two uterine arteries exist, there is no proof that these anastomoses are functional.

When the placenta is laterally located, the uterine artery close to the placenta has lower resistance than the one opposite from it. In patients with centrally located placentas both uterine arteries demonstrate similar resistance.^{14,20} It is possible that when the placenta is centrally located, the uteroplacental blood flow needs are met by equal contribution from both uterine arteries. However, when the placenta is laterally located, in the majority of patients the uteroplacental blood flow needs are to be met primarily by one of the uterine arteries, with some contribution by the other uterine artery via collateral circulation. The degree of collateral contribution, however, may not be the same in all patients and deficient contribution may facilitate the development of preeclampsia, IUGR, or both. The existence of major vascular anastomoses in some patients may explain the normal uterine artery flow velocity waveforms and the absence of preeclampsia and IUGR despite the presence of a unilateral placenta.

The pathophysiologic characteristics of preeclampsia are complex and the cause remains unknown. One of the fundamental disturbances in patients with this condition is decreased uteroplacental blood flow. However, whether this is the cause or the result of preeclampsia is yet to be discovered. Our data indicate that the presence of a unilateral placenta and abnormal uterine artery flow velocity waveforms (suggestive of high uterine artery resistance) is strongly associated with preeclampsia. Studies are currently being conducted both in the United States and abroad to evaluate the impact of aspirin in the prevention of preeclampsia. Further studies are necessary to evaluate the sensitivity of placental laterality and abnormal uterine artery flow velocity waveforms as a predictor of the development of preeclampsia. If this proves to be the case, the use of aspirin in those patients who are at increased risk will help prevent or at least ameliorate some of the severe consequences of preeclampsia.

In summary, this study is the first to demonstrate a significant relationship between placental laterality and the presence of preeclampsia, IUGR, or both. There is strong evidence to indicate that patients with unilateral

placentation are more likely to have abnormal uterine artery flow velocity waveforms indicative of high uterine artery resistance. It is speculated that insufficient collateral blood supply in patients with unilateral placentation may facilitate the development of preeclampsia, IUGR, or both. Further study of this relationship is needed to evaluate its sensitivity as a screening tool for patients at risk to develop preeclampsia or IUGR.

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