J Obstet Gynecol Cancer Res. 2017 November; 2(4):e11945. doi: 10.5812/jogcr.11945.
Published online 2017 September 27. **Research Article**

Prediction of Pre-Eclampsia Development by Placenta Location: A Simple Predictor

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Received 2017 August 28; **Accepted** 2017 August 29.

Abstract

Background: Pre-eclampsia complicates 5% to 8% of all pregnancies and annual incidence of pre-eclampsia is about 5% of all pregnancies around the world and is a significant cause of both maternal and fetal mortality and morbidity if left untreated.
Objectives: According to previous studies, blood supply distribution within the uterus is not similar in central compared with lateral sites, thus site of implantation and the resulting location of the placenta are likely to have a profound effect on the pregnancy outcome.
Methods: The researchers conducted a case-control study over 1-year period at a referral obstetric hospital in the south of Tehran. Overall, 121 females with three degrees of pre-eclampsia were considered as cases and 258 females with normal pregnancy were the controls. The females were aged 20 to 40 years old and their gestational age was between 14 and 26 weeks.
Results: The researchers recorded the participants' blood pressures and locations of placenta during this period with consideration of their past and present obstetric history as well as medical and familial history. As a result, pregnancies complicated by pre-eclampsia were more commonly associated with lateral placentation in the second trimester when compared with non-pre-eclampsia pregnancies.
Discussion: This study suggests that placental location, which is easily assessed at middle trimester of pregnancy by routine screening ultrasonography, is an ideal predictive test for evaluating the risk of developing pre-eclampsia.

Keywords: Pre-Eclampsia, Placenta Location

1. Background

Pre-eclampsia is defined as new hypertension with systolic blood pressure of more than 140 and diastolic pressure of 90 mmHg after 20 weeks of gestational age together with proteinuria (more than 0.3 g/24 hours), which could complicate 5% to 8% of all pregnancies and if remained untreated leads to major mortality and morbidity. Ten million pregnant females are complicated by pre-eclampsia each year around the world, which is 7 folds higher in developing countries (1). The exact etiology of pre-eclampsia is unknown, yet it is thought to be associated with abnormal blood flow of placenta. Potential complications of pre-eclampsia include a lack of proper placental blood supply resulting in intrauterine fetus growth retardation and premature delivery, premature detachment of placenta, HELLP syndrome, eclampsia, and cardiovascular diseases. Recent evidence suggests the assessment of some factors in the first trimester, such as resistance index of uterine artery (RI index) and serum markers, such as HCG or PAPP-A (2).

Based on previous investigations, blood distribution is different in central and lateral parts of the uterus, and placenta location has a major role in prediction of pregnancy outcomes. It has been suggested that placental location plays a role in premature delivery, mal presentation, and development of pre-eclampsia. As a life-threatening disease, in the developing world, 10% to 25% of affected mothers die from pre-eclampsia and related hypertensive disorders, hereby it should be detected early and managed appropriately before onset of complications. In preliminary investigations by Wood et al. in 1962 (3) and Friedman et al. in 1964 (4), different methods, such as X-ray imaging of soft tissue, were used to determine placental location and their potential association with pre-eclampsia.

By emergence of sonography, different investigations have been performed to assess the association between the locations of lateral placenta and occurrence of pre-

eclampsia in pregnancy; Cophianes et al. showed that lateral placenta is more likely to be associated with abnormal fetus blood supply, and that the lateral placenta is considered a predisposing factor for pre-eclampsia incidence and intra-uterine growth retardation (IUGR). Zhong et al. in 2010 also proposed Color Doppler US and assessment of the level of serum markers as predictive tests for prediction of pre-eclampsia and IUGR (5). Another investigation by Chhabra et al. in 2013 showed a meaningful difference regarding pregnancy outcomes considering place and size of placenta in the first trimester of pregnancy (6).

In another study by Kalanithi et al. in pregnancies with IUGR, central placenta was found 4 times more than those with normal pregnancy (7).

However, Guiot et al. in 2008 proposed US as a non-invasive modality to predict pre-eclampsia. Despite the mentioned findings, there is paucity of data regarding the association of placental location and occurrence of pre-eclampsia in the literature (8).

On the other hand, development of pre-eclampsia leads to abnormal placental blood flow and is a potential source of ill-being pregnancy outcomes, such as fetal growth restriction as well as preterm birth and stillbirth of the fetus (6-12).

In the United States, as a developed country, only 80% of mothers are familiar with Pre-eclampsia with low awareness of hypertension symptoms (13). Regarding the global burden of Pre-eclampsia (1, 4), screening programs during pregnancy are essential, yet in countries with lower social status, frequent prenatal evaluations are not certain, thus a simple predictor of Pre-eclampsia to use for early detection is required.

Regarding previous studies, blood supply distribution within the uterus is not of a similar form in central versus lateral sites implicating that site of implantation and resultant location of the placenta are likely to have a profound effect on the pregnancy outcome (6-12). In addition, previous studies have revealed side-to-side differences in uteroplacental Doppler flow in pregnancies with unilateral placentas as well as the relationship between abnormal Doppler measurements and pre-eclampsia (14-21). However, reports on the direct association between placental location and development of pre-eclampsia, regardless of confounding factors (22), are limited.

The current study was conducted to investigate placental location in routine ultrasonographic exam, performed at second trimester of pregnancy, and determine whether this could be a simple predictor of development of pre-eclampsia in the third trimester.

The researchers organized a retrospective case-control study in singleton pregnancies with (n = 121) and without (n = 258) pre-eclampsia to assay the association between development of pre-eclampsia in third trimester and second-trimester placental location.

2. Objectives

This study was done to determine placental location, which is easily assessed during the middle trimester of pregnancy by routine screening ultrasonography, as an ideal predictive test for evaluating the risk of developing pre-eclampsia.

3. Methods

3.1. Study Design and Population

This was a case-control study of singleton pregnancies with (n = 177) and without (n = 270) pre-eclampsia to assay the association between development of pre-eclampsia in the third-trimester and second-trimester placental location.

This retrospective study was done based on the data of patient records, which received pre-natal care at the Mahdiyeh hospital, admitted between April 1st, 2012 and April 1st, 2013.

With consideration of the exclusion criteria, 121 pre-eclampsia cases and 258 controls were identified.

All selected cases and controls were having singleton pregnancies and had performed at least one second-trimester sonographic examination (range, 14 to 26 weeks). Pregnancies with pre-eclampsia were separated in a special subgroup of pre-natal care, considering persistently high blood pressure after 20 weeks of gestation associated with a high level of protein in urine, low platelet count and other signs of organ failure, such as fluids in the lungs, and trouble with the kidneys or liver.

The researchers excluded patients with persistent abnormal blood pressure between 14 and 20 weeks of gestation (n = 28), and patients that had delivered at another location or with incomplete data, such as lack of maternal history, fetal weight, and type of delivery (n = 28).

Cases were selected according to the inclusion criteria.

Control cases were those with pregnancies that had no evidence of pre-eclampsia in their prenatal cares and at least one sonographic exam during the second trimester (range, 14 to 26 weeks). Data were collected in special forms. Data was analyzed using EXCEL. Multivariate logistic regression was used to analyze the data.

2. Definition According to the new guideline, revised by the American college of obstetricians and gynecologists (ACOG), including the notes of the world health organization (WHO) and the society of obstetricians and gynecologists of Canada (SOGC), pre-eclampsia is diagnosed as a persistently high blood pressure during pregnancy associated

with evidence of organ problems, with or without proteinuria (2, 3).

Placental location reported by the sonographic examination was defined in the following 5 groups: anterior, posterior, fundal, right lateral, and left lateral.

3.2. Statistical Analysis

Results Pre-eclampsia cases and no pre-eclampsia cases did not differ with respect to gravity and parity; differences of about 2 years were detected between cases and controls (Table 1).

The groups had comparable proportions of mothers with underlying disease, including hypertension (2.5% of pre-eclampsia vs. 0.4% of control, P value: 0.98), which revealed no significant difference, yet the number of mothers with diabetes mellitus in pre-eclampsia pregnancies was twice that of the group with normal pregnancies (16.5% of pre-eclampsia vs. 8% of control-value : < 0.001) with the difference being significant.

Except previous history of pre-eclampsia, the presence of other reported risk factors for pre-eclampsia, including smoking, previous history of IUFD/IUGR as well as family history of pre-eclampsia were negligible.

In evaluation of previous history of pre-eclampsia and IUFD/IUGR, only mothers with gravity greater than 1 time were included. Distribution of moderate and severe pre-eclampsia in different placental locations has been mentioned in Table 2. As indicated, the most frequent location of placenta was the anterior area in the 2 groups. For better analysis, the researchers categorized placental locations to 2 groups as lateral and other locations. In addition, they combined moderate and severe pre-eclampsia as one group of pre-eclampsia (versus normal subjects). Then, these 2 groups were analyzed against each other to find out if the distribution of the pre-eclampsia is different between the 2 groups of laterally located placentas versus other locations. Analysis showed lateral placenta was associated with pre-eclampsia in 47.6% (20 out of 42) of cases while other locations were associated with pre-eclampsia in 30% (101 out of 337) (P Value = 0.02, Odds ratio: 2.1, 95% confidence interval: 1.1 - 4.1). In the pre-eclampsia group, right lateral placenta and in the normal group, left lateral placenta were more commonly observed.

In the pre-eclampsia group, 80% of females underwent cesarean section compared to 66.5% in the normal group, which yielded a significant difference (P = 0.005). Similarly, low birth weight (below 2500 g) in the pre-eclampsia group was 47.3% while this was 4.7% in normal subjects (P < 0.001). The mentioned data revealed that pre-eclampsia pregnancies had more antepartum and intrapartum complications than the non-pre-eclampsia group (Table 3).

4. Discussion and Conclusion

The earliest studies on the association between placental location and pre-eclampsia were done by Booth et al. (1962) (23) and Little et al. (1964) (24), based on manual exploration of the uterus and soft tissue X-ray film, with controversial results and the association between the pre-eclampsia and IUGR, as a confounding factor. After advances in ultrasound examinations, studies were done upon the association between fundal location of placenta and abnormal placental blood flow. A study by Kofinas et al. (1989) reported a relationship between the lateral location of the placenta and the development of preeclampsia and IUGR as well as abnormal resistive index of the uterine artery in lateral placentas, without respect to confounding factors, such as risk factors for development of preeclampsia (21). According to an important study done by Bhalerao et al. during year 2013, ultrasound has been shown as a cost-effective method for prediction of the development of preeclampsia (17), yet in this recent study, statistical analysis of lateral placentas in cases with underlying diseases and older mothers were not apparent.

The current retrospective case-control study, according to statistical results (with respect to valuable variables associated with pre-eclampsia), multi-variable logistic regression analysis between maternal age, high-body mass index, diabetes mellitus and lateral location of placenta as independent variables and development of pre-eclampsia as a dependent variable demonstrated that age, diabetes mellitus, and lateral location of placenta were associated with each other with a significant difference.

This means lateral location of placenta is an independent predictor of development of preeclampsia, consistent with recent studies.

In assessing the placental location, lateral placenta had a meaningful effect with odds ratio of 2.1 in complicated deliveries with pre-eclampsia compared to normal deliveries. Besides, cesarean section and low birth weight were more commonly seen in the pre-eclampsia group compared to the normal group.

Overall, the current study showed that lateral placenta (non-central) was more commonly seen in deliveries complicated with pre-eclampsia compared to normal deliveries. However, the current study verified that lateral placenta was more commonly related to inappropriate complications of delivery, such as low birth weight and cesarean section.

Ultrasound as a safe, available, and accurate method in routine prenatal care is a simple predictor of pre-eclampsia and pregnancies with lateral placenta should be managed by close visits to detect high blood pressure early in gestation before organ damages.

Table 1. Characteristics of the Study Population

	Pre-Eclampsia Group (N = 121, 31.9%)	Normal Group (N = 258, 68.1%)	P Value		Confidence Interval
Mean mother age	26.8 ± 5.9	29.0 ± 5.9	0.001		
Previous gestation number	2.1 ± 1.2	2.3 ± 1.2	0.137		
Previous delivery number	0.8 ± 1	0.9 ± 1	0.37		
Morbid obesity	3 (2.5)	0%?	0.032		
Cigarette smoking	1 (0.8)	0%?	0.32		
Pre-eclampsia history	15 (19)	2 (1.2)	< 0.001	18.1	3.9 - 80.1
IUGR history	4 (3.3)	0%?	0.01		
Pre-eclampsia familial history	0%?	0%?	-		
Diabetes history	20 (16.5)	8 (1.3)	< 0.001	6.2	2.6 - 14.5
HTN history	3 (2.5)	1 (0.4)	0.98	6.5	0.67 - 63

Table 2. Distribution of Moderate and Severe Pre-eclampsia in Different Locations of the Placenta

Placenta Location		Normal	Moderate	Severe
Right Lateral	Count	12	4	10
	Percent	46.2	15.4	38.5
Left Lateral	Count	10	3	3
	Percent	62.5	18.8	18.8
Posterior	Count	98	16	21
	Percent	72.6	11.9	15.6
Anterior	Count	104	22	34
	Percent	65.0	13.8	21.3
Fundal	Count	34	7	1
	Percent	81.0	16.7	2.4

Table 3. Comparison of Placenta Location, Cesarean Section and Low Birth Weight in Pre-eclampsia versus Normal Subjects

	Lateral location	C/S	IUGR
Pre-eclampsia	20 (16.5)	92 (80)	53 (47.3)
Normal	22 (8.5)	171 (66.5)	12 (4.7)
P Value	0.021	0.008	< 0.001
Odds Ratio (95% Confidence interval)	2.1 (1.1 - 4.1)	2 (1.2 - 3.4)	18.3 (9.2 - 36.5)

Finally, it is suggested to perform more investigations with Doppler US of placental location in 2 groups of normal and lateral placenta to find more evidence in this regard.

Acknowledgments

The authors would like to express their special thanks to the patients, who provided the opportunity to perform this project on the topic (prediction of developing pre-eclampsia by placental location: A simple predictor). Secondly they would also like to thank those who assisted with finalizing the project.

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