Utility of Placental Laterality and Uterine Artery Doppler Abnormalities for Prediction of Preeclampsia

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Received: 30 July 2015 / Accepted: 21 December 2015 / Published online: 26 February 2016
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Abstract

Objective To find out whether placental laterality and abnormal uterine artery waveform and resistance index, as determined by antenatal ultrasonography and Doppler, can be used as a predictor for the development of preeclampsia.

Methods This prospective observational cohort study was conducted from August 2013 to October 2014. Two hundred and one (201) normotensive, primigravida women with singleton pregnancies attending the antenatal clinics without any high-risk factor for development of hypertension were subjected to ultrasonography at 18–22 weeks of gestation to determine the placenta location. All the subjects with lateral placentas were subjected to Doppler ultrasonography to look for abnormal Doppler waveform and resistance index. They were followed for the development of preeclampsia till 40 weeks of gestation or delivery.

Result Out of the total 201 women, 71 (24.5 %) had laterally located placentas and of them 37 (52 %)

developed preeclampsia, while the remaining 130 (75.5 %) had centrally located placentas and of them 14 (10.8 %) developed preeclampsia ($p < 0.001$). In subjects with lateral placentas alone ($n = 33$), 2 (6 %) developed preeclampsia while as those with lateral placentas with Doppler abnormality ($n = 38$), 35 (92 %) developed preeclampsia ($p < 0.001$). The overall risk of developing preeclampsia with laterally located placenta was 9.27 (odds ratio), and 95 % confidence interval was (4.30–19.98).

Conclusion Pregnant women with lateral placentas are at significant risk for development of preeclampsia. Lateral placentas when associated with uterine artery Doppler abnormality, risk for development of preeclampsia increases significantly as compared to lateral placentas alone.

Keywords Placental laterality · Preeclampsia · Placenta · Abnormal Doppler waveform

Background

The precise pathogenesis of preeclampsia remains to be a subject of extensive research, but it is believed that it is likely to be multifactorial. The factors currently considered to be most important include maternal immunological intolerance, abnormal placental implantation, genetic, nutritional and environmental factors and cardiovascular and inflammatory changes [1]. Nevertheless, it is accepted that it is the presence of the placenta rather than the fetus, which is responsible for development of preeclampsia. Recent research related to the placental transcriptome profile in preeclampsia is strongly in favor of placental origin of preeclampsia [2].

The placenta is located laterally in majority of patients with abnormal flow velocity waveforms. Impaired trophoblastic invasion of uterine spiral arteries is involved in the etiology of preeclampsia, and persistent high resistance in the uterine arteries (UtAs) reflects the etiology process. The latter finding has been used as a proposed screening strategy for preeclampsia using Doppler assessment of both uterine arteries in the first and second trimesters [3, 4]. This study was designed to find out the relation of placental laterality and uterine artery Doppler abnormalities to the development of preeclampsia.

Subjects and Methods

This prospective observational study was conducted at Post Graduate Department of Gynecology and Obstetrics, Sheri Kashmir Institute of Medical Sciences, Srinagar, which is a

tertiary care teaching institute in the state of Jammu and Kashmir. This study was conducted between August 2013 and October 2014 including complete follow-up of the last case registered for the study. A written informed consent was obtained from all the participants at the time of enrollment for the study.

Inclusion Criteria

Normotensive, primigravida women with singleton pregnancies, attending antenatal clinics at 18–22 weeks of gestation were included.

Exclusion Criteria

Pregnant women with diabetes, hypertension, renal disease, collagen vascular disorders or with history of smoking were excluded.

Mid-trimester (18–22 weeks) blood pressures were recorded by auscultatory method in all the eligible pregnant subjects. Location of the placenta was determined by real-time ultra-sonography. Ultra-sonography was performed using Aloka Pro-sound SSD-3500FX ultrasound machine using 3.5 MHZ transducer. Lateral placenta was considered to be present only when 70 % or more of the placenta was on one side of the uterine cavity. All patients with lateral placentas were subjected to color Doppler to find out the uterine artery resistance index and abnormal notching in placental artery. Uterine artery resistance index of more than 0.56 and presence of protodiastolic notch in the placental ipsilateral side in uterine artery were taken as significant. All subjects were followed till 40 weeks of gestation for occurrence of preeclampsia as per ACOG (American College of Obstetrics and Gynecology) guidelines [1]. Those patients who delivered before 40 weeks but after 37 weeks were also included in the final analysis irrespective of development of preeclampsia. Mothers who delivered before 37 weeks but developed preeclampsia at any time after enrollment were also included in final analysis.

Results

Demographic and other baseline characteristics of our study population are depicted in Table 1. Placenta location and abnormal Doppler incidence are depicted in Table 2. Incidence of preeclampsia is given in Table 3. Binary logistic regression analysis (multivariate analysis) for the dependent variables of preeclampsia is given in Table 4.

Statistical Analysis

All are the continuous variables so the study has been shown in terms of descriptive statistics and the categorical variables in terms of frequency and percentages. The data were analyzed with the help of Chi-square test for univariate cases, and the binary logistic regression analysis has been employed for multivariate analysis. All the results obtained have been discussed on 5 % level of significance, i.e., p value less than 0.05 considered significant. The data were analyzed with SPSS V.20.

Discussion

In our study, we found that the subjects with lateral placentas have significantly higher risk of developing preeclampsia as compared to those who have central placentas ($p \leq 0.001$). We also observed that the subjects having lateral placentas along with Doppler abnormality have more risk of developing preeclampsia on follow-up as compared to those who have lateral placentas alone ($p \leq 0.001$). After logistic regression we observed that in subjects with lateral placentas, the overall risk of developing preeclampsia is 9.27 (odds ratio). The strengths of our study are: Out of 228 subjects who were enrolled for the study, just 4 (1.7 %) were lost to follow-up. Two hundred and one (88.2 %) subjects were available for final analysis (23 delivered before 37 weeks of gestation and before development of preeclampsia), and no dropouts were included in the final analysis. Logistic regression model was utilized for final analysis in order to eliminate the effect of confounding factors. The limitation of our study is that it is an observational cohort study and not a randomized controlled trial. However randomization was not possible because of the nature of the study.

In our study, out of 201 subjects, 71 (24.5 %) were with lateral placentas and 130 (75.5 %) patients were with central placentas. Out of 71 subjects with lateral placentas,

37 (52 %) developed preeclampsia, and out of 130 subjects with central placenta, just 14 (10.8 %) developed preeclampsia. The difference was statistically significant ($p \leq 0.001$).

Our findings are consistent with the findings of Tania Kakker et al. [5] who observed that out of 150 women, 84 (56 %) had laterally located placentas and of them 56 (66.6 %) developed preeclampsia ($p < 0.00002$). Our findings are also in accordance with the findings of Fung et al. [6] who performed a retrospective study on 16236 patients having ultrasound examination at 14 to 23 weeks of gestation. Non-central placental location in the second trimester was associated with an increase risk of adverse obstetric outcomes including preeclampsia [OR = 2.27; 95 % confidence intervals (CIs), 1.31–3.93]. Secken et al. [7] also found preeclampsia significantly higher in the lateral placental location group (4.5 vs. 1.6 %; $p = 0.027$).

In our study, 2 (6 %) out of 33 with lateral placentas alone developed preeclampsia while as 35 (92 %) out of 38 with lateral placentas with Doppler abnormalities developed preeclampsia ($p < 0.001$). Joni et al. also reported similar findings. They observed that out of 400 cases enrolled, 80 (20 %) cases had lateral placentas on ultrasound examination done at 18–24 weeks of gestation. Out of the 80 women with laterally located placenta, 28 (35 %) developed preeclampsia, which was statistically significant. A total of 26 subjects were having raised uterine artery resistance and out of them 22 (84 %) developed preeclampsia; out of remaining 54 women, only 6 (11 %) developed preeclampsia ($p < 0.001$) [8]. Alpesh et al. observed that 14 (35 %) out of 40 subjects having lateral placenta developed preeclampsia ($p < 0.001$). Out of all 40 subjects having lateral placenta who underwent color Doppler, 13 patients had raised uterine artery resistance index ($p < 0.001$). They concluded that lateral placenta can be used as a predictor marker for preeclampsia, and if all patients with lateral placenta undergo color Doppler, preeclampsia can be predicted more accurately [3]. Other researchers including Negar et al. [9], Pagani et al. [10],

Table 1 Demographic and other baseline characteristics

Attribute ($N = 201$)	Minimum/maximum	Mean/median/inter quartile range	No. of subjects (%age)
Age in years	19/40	25.36/25/5	201 (100)
Gestation at screening (weeks)	18/21	19.23/19/2	201 (100)
Urban			66 (32.8)
Rural			135 (67.2)
Assisted reproductive technology			5 (2.5)
Primary infertility			15 (7.5)
Secondary infertility			0(0)
Diabetes, hypertension, renal disease, collagen vascular disease, smoking			0(0)

Table 2 Location of the placentas and abnormal Doppler incidence

Lateral placenta (No./percentage)	Central placenta (No./percentage)	Lateral placenta without Doppler abnormality (No./percentage)	Lateral placenta + Doppler abnormality (No./percentage)	Total (No./percentage)
71 (24.5)	130 (74.5)	33 (16.4)	38 (18.9)	201 (100)

Table 3 Incidence of preeclampsia as a function of different variable

Placenta location		Preeclampsia	p value
	Lateral ($n = 71$)	37 (52 %)	<0.001
	Central ($n = 130$)	14 (10.8 %)	
Age group	19–30 years ($n = 181$)	46 (25.4 %)	0.968
	30–40 years ($n = 20$)	5 (25 %)	
Urban	$n = 66$	16 (24.2 %)	0.797
Rural	$n = 135$	35 (25.9 %)	
Assisted reproductive technique	$n = 5$	3 (60 %)	0.10
Spontaneous conception	$N = 196$	48 (24.5 %)	
Primary infertility	$n = 15$	9 (60 %)	0.003
No infertility	$n = 186$	42 (25.6 %)	
Lateral placenta alone	$n = 33$	2 (6 %)	<0.001
Lateral placenta with Doppler abnormality	$n = 38$	35 (92 %)	
Central placenta only	$n = 130$	14 (10.4 %)	<0.001
Lateral placenta with abnormal Doppler	$n = 38$	35 (92 %)	

Table 4 Binary logistic regression analysis (multivariate analysis) for the dependent variable preeclampsia

Variable	Wald	p value	Odds ratio	95 % confidence interval for odds ratio Lower–upper
Age (19–30)	2.668	0.102	7.632	0.666–87.435
Residence (rural)	0.638	0.425	1.419	0.601–3.352
ART (No)	1.450	0.228	0.167	0.009–3.076
P.INF (yes)	6.288	0.012*	18.156	1.883–75.024
Placenta (Lateral)	32.364	<0.001*	9.275	4.306–19.978
Constant	3.029	0.082	0.065	

* p value significant

Ventura et al. [11], Ohkuchi et al. [12], Mose [4], Roeder et al. [13] and Napolitano et al. [14] have also found significant association of abnormal antenatal Doppler abnormalities with development of preeclampsia on follow-up.

In addition, we observed that primary infertility ($p = 0.003$) and lateral placenta ($p < 0.001$) are independent risk factors for preeclampsia. After logistic regression, it was found that the overall risk of developing preeclampsia with laterally located placenta is 9.27 (odds ratio) with 95 % confidence interval of (4.306–19.978). Tania et al. also observed that the overall risk of developing preeclampsia with laterally located placenta is 5.09 (odds ratio) and 95 % confidence interval of (2.40–10.88).

Conclusion

Pregnant women with lateral placentas are at significant risk for development of preeclampsia. Lateral placentas when associated with uterine artery Doppler abnormality, risk for development of preeclampsia increases significantly as compared to lateral placenta alone.

Author contributions SY involved in review of literature and data collection and wrote the first draft; SHT involved in designing of study, drafting the article, analysis and interpretation of data. He is and will act as guarantor; AA, SQ, SG, FS and SA involved in designing of study, collection of data and drafting the manuscript. RD involved in analysis and interpretation of data. The final manuscript was approved by all the authors.

Compliance with Ethical Standards

Conflict of interest All the authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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