Original Article

Placental Laterality as a Predictor of Preeclampsia

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ABSTRACT

Objective: To study whether ultrasonically identified, placental laterality can be used as a predictor for development of preeclampsia.
Materials and Methods: This prospective study was conducted in the Department of Obstetrics and Gynecology, Chalmeda Ananda Rao Institute of Medical Sciences, Bommakal, Karimnagar from 2013 to 2014. 300pregnant women attending antenatal clinic both OPD and IPD at 18 *to* 24 weeks of gestation without any high risk factor were subjected to ultrasound examination, and placental location was determined. These cases were followed for the development of signs and symptoms of preeclampsia.
Results: Out of the total 300 women, 168 (56 %) had laterally located placenta and of them, 112 (66.6 %) developed preeclampsia, while the remaining 112 (44 %) had centrally located placenta and of them, 48 (36.3 %) developed preeclampsia. So, the overall risk of developing preeclampsia with laterally located placenta was 5.09 (odds ratio) and 95 % confidence interval (2.40 *to* 10.88). The difference was found to be statistically significant, p value (0.00002) by chi-square test.
Conclusion: Ultra sonography is simple, non invasive, easy to perform, cost effective, diagnostic method to identify high risk cases. From the above study, we concluded that females with laterally located placenta determined by USG at 18 *to* 24 weeks of gestation have five times greater risk of developing preeclampsia. By identifying such patients appropriate treatment can be initiated and the patient's are regularly followed up.

Keywords: Placental laterality, Preeclampsia, Central placenta.

INTRODUCTION

Preeclampsia is a multi-system disorder of pregnancy, which is characterized by new onset hypertension (systolic and diastolic blood pressure of ≥ 140 and 90 mm Hg, respectively, on two occasions, at least 6 hours apart) and

proteinuria (protein excretion of ≥ 300 mg in a 24 hr urine collection, or a dipstick of ≥ 2+), that develop after 20 weeks of gestation in previously normotensive women.

Preeclampsia occurs only in the presence of placenta[1]. Several tests have been proposed to identify women at risk of developing preeclampsia. Some of these tests such as the cold pressor test, the isometric hand grip exercise, and the roll over test depend on the presence of some pathophysiological changes that occur in preeclampsia. Other tests such as the measurement of urinary calcium or plasma fibronectin are based on the presence of biochemical alterations peculiar to this disease. Placental location has been found to correlate with fetal position and presentation[2,3], length of gestation[4], course of labour[5], presence of preeclampsia[6,7], and pregnancy outcome[8].

Among the various predictors for preeclampsia, the placental location by ultrasound at 18 to 24 weeks is very cost effective, noninvasive, and has a good positive predictive value[9]. There is a significant association between placental location and uterine artery resistance and adverse outcomes such as preeclampsia and IUGR[10]. In the women with centrally located placenta, both uterine arteries demonstrate similar resistance. When the placenta is laterally located, the uterine artery close to the placenta has lower resistance than the one opposite from it. In laterally located placenta, 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[10,11]. The degree of collateral contribution may not be the same in all women, and deficient contribution facilitates the development of preeclampsia, IUGR, or both.

MATERIALS AND METHODS

The present study is a prospective study. This study was carried out in the Department of Obstetrics and Gynecology, Chalmeda AnandRao Institute of Medical Sciences, Karimnagar, Telangana from October 2013 to 2014.

Inclusion criteria

All pregnant women attending the antenatal clinic, both outpatient and ward admissions, at 18 to 24 weeks of gestation without any high risk factors were included in this study.

Exclusion criteria

Pregnant women were excluded from the study if they were having chronic hypertension or essential hypertension, diabetes mellitus, thyrotoxicosis, renal disease, severe anemia, connective tissue disorder, positive lupus anticoagulant anti-cardiolipin antibodies, RH incompatibility, twin pregnancy, or positive VDRL test.

All the cases were subjected to detailed history, general physical, and systemic as well as obstetrical examination at the time of their antenatal visit and at the time of admission. The location of placenta was determined by ultrasound at 18 to 24 weeks in all the selected women and followed subsequently for the development of preeclampsia. The placenta was classified as central when it was equally distributed between the right and left side of uterus irrespective of anterior, posterior, or fundal position. When 75 % or more of the placental mass was to one side of the midline, it was classified as unilateral right or left placenta.

All women were followed throughout the pregnancy for the development of the signs and symptoms of preeclampsia. Preeclampsia was diagnosed on the basis of the American Congress of Obstetricians and Gynecologists criteria for

preeclampsia. The patients were treated according to the severity of the disease.

Mild preeclampsia

Reduce the level of activity, monitor and have frequent visits and testing.

Moderate to severe preeclampsia

Expectant management includes bed rest, Anti-hypertensive drugs can only lower the blood pressure but will not stop preeclampsia from worsening or reduce the risks of its complications, corticosteroids for lung maturation if < 34 weeks and close monitoring of both mother and fetus.

Severe preeclampsia or eclamptic seizure

Magnesium sulfate to treat in case of eclampsia and also prevent from eclampsia in cases of severe preeclampsia, corticosteroids for lung maturation if < 34 weeks, in severe cases with persistent hypertension, pregnancy was terminated.

Delivery

Vaginal delivery is safest, if preeclampsia is getting worse or fetal monitoring suggests fetal distress or any obstetric indication cesarean section is planned.

RESULTS

Out of the total 300 women, 60 % (180) were in the age group 21 to 25 years (Table 1). 168 (56 %) cases had laterally located placenta, while 132 (44 %) cases had centrally located placenta on ultrasound examination done at 18 to 24 weeks of gestation (Table 2). Out of the 168 women with laterally located placenta, 112 (66.6 %) developed PIH, while 48 women (36.3 %) out of the remaining 132 women with centrally located placenta developed PIH. So, the risk of developing PIH was five times greater in the females with laterally located placenta as compared to those with centrally located placenta. The overall risk of developing PIH with laterally located placenta was 5.09 (odds ratio) and 95 % confidence interval (CI) 2.40 to 10.88. The difference was found to be highly significant statistically ($p = 0.00002$ by chi-square test).

Out of the total 300 cases, 78 developed mild PIH (D.B.P 90 to 99 mmHg). Out of these 78 cases, 32 had centrally located placenta and 46 had laterally located placenta (Tables 3, 4). Fifty -Four women developed moderate PIH (D.B.P 100 to 109 mmHg). Out of these 54 cases, 14 had centrally located placenta, while 40 women had laterally located placenta (Tables 3, 4). Twenty eight women developed severe PIH (D.B.P>110 mmHg) and out of these 2 had centrally located placenta and 26 had laterally located placenta. No case of eclampsia was reported (Tables3, 4).

DISCUSSION

Preeclampsia is a complex clinical syndrome involving multiple organ systems and still remains the principal cause of maternal and perinatal mortality and morbidity[12]. It has been shown that in humans, both uterine arteries have a significant number of branches and each supply the corresponding side of the uterus. Although anastomoses between the two uterine arteries exist, there is no proof that these 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 placenta, both uterine arteries demonstrate similar resistance[10,11,13]. 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 the patients, the uteroplacental blood flow needs are to be met primarily by one of the uterine arteries, with some contribution by the other uterine

arteries, with some contribution by the other uterine artery via collateral circulation. This degree of collateral circulation, however, may not be the same in all patients and deficient contribution may facilitate the development of preeclampsia, IUGR or both[14].

The existence of major vascular anastomoses in some patients may explain the normal uterine flow velocity waveform and absence of preeclampsia and IUGR despite the presence of a unilateral placenta. In normal pregnancies, the spiral arterioles that supply the placental bed undergo trophoblast induced conversion to uteroplacental arterioles. The significance of normal placentation for this cytotrophoblastic invasion is high and the cytotrophoblasts fail to adopt a vascular adhesion phenotype in preeclampsia[15]. In preeclampsia conversion of the spiral arterioles is incomplete[16]. It involves only the subplacental veneouls. If there were no functional anastomoses between right and left uterine arteries, in cases with unilaterally located placentas, one would expect the ipsilateral uterine artery systolic/ diastolic ratios to change more than the contralateral ratios in hypertensive pregnancies. This may explain the reduced trophoblastic invasion in laterally situated placenta when the uteroplacental blood flow need are mainly met by one side uterine artery.

Potential biochemical markers for the prediction (1st trimester, 2nd trimester) or detection of preeclampsia in maternal peripheral blood are identified. they are soluble fms-like tyrosine kinase 1(sflt-1), soluble Endoglin (sEng),: placental growth factor (PlGF),: Placental protein 13(PP-13), Pentraxin 3(PTX3), P-selectin, Cell free fetal DNA, Adrenomedullin, Auto antibodies against the angiotensin II type 1 (AT1) receptor, recent biomarkers are Visfatin (nicotinamide phosphoribosyltransferase (Nampt) enzyme these are used to detect preeclampsia at earlier stage of disease.

In the present study, out of 300 women, 168 (56 %) females had laterally located placenta and 132 (44 %) had centrally located placenta. Out of the 168 women with laterally located placenta, 112 (66.6 %) developed PIH as compared to 132 females with centrally located placenta where 48 (36.6 %) developed PIH. So, the risk of developing PIH was five times greater for the females with laterally located placenta as compared to those with centrally located placenta. The overall risk of developing PIH with laterally located placenta was 5.09 (odds ratio) and 95 % CI 2.40 to 10.88. The difference was found to be highly significant statistically (p = 0.00002). This result is in accordance with Kofinas *et al*.[17] who concluded that in women with unilateral placenta, the incidence of preeclampsia was 2.8-fold greater than those with centrally located placenta. The results of the present study were also comparable to those of Muralidhar *et al*.[18]. In his study, a total of 426 unselected singleton pregnant women were included. Out of 426 women, 324 had centrally located placenta and 102 had unilateral placenta. A total of 71 women developed preeclampsia of which 52 (74 %) had unilaterally located placenta. The relationship was found to be statistically significant p\0.0001. The results of the present study were also comparable to the study done by Lucy *et al*.[19], the results of which showed that development of PIH and IUGR pregnancies were nearly fourfold more in lateral placentation.

Despite extensive clinical trials, up to date, no therapeutic approaches are available for either treatment or prevention of preeclampsia. Anti-hypertensive drugs, corticosteroids for lung maturation or magnesium sulfate to prevent from eclampsia (RCOG Guideline No. 10(A)) are to prevent the worsening of the symptoms and can thus temporize over the short term to allow for safe delivery with a more mature fetus. Several prophylactic therapies (anti-oxidant

vitamins, calcium or folic acid supplementation, Aspirin) have so far failed to prove efficacious in the prevention of preeclampsia in healthy, nulliparous subjects, although some benefit has been shown in high risk groups. The only cure of preeclampsia is delivery of placenta and baby.

Risk of recurrent preeclampsia is between 5 to 70 percent. women who had severe features of preeclampsia and were delivered before 30 weeks gestation having the highest risk up to 70 percent in future pregnancies. Women with preeclampsia without severe features have only 5 percent chance of developing preeclampsia.

CONCLUSION

Ultrasonography is simple, non invasive, easy to perform, cost effective, diagnostic method to identify high risk cases. From the above study, it is concluded that laterally located placenta on ultrasound done at 18 *to* 24 weeks is associated with increased risk of development of preeclampsia. Females with laterally located placenta have a five times greater risk of developing PIH, so these pregnancies may require careful obstetric management to achieve a more favorable outcome and decrease the maternal and perinatal morbidity and mortality associated with preeclampsia.

ACKNOWLEDGEMENT

The authors are thankful to the patient and her attendants for their consent to publish the case and are grateful to chairman Sri Chalmeda Lakshmi Narasimha Rao Director Dr. V. Suryanarayana Reddy and Dr. Shanmuga Raju I/C HOD & Assoc. Professor of Physiotherapy for their constant support and encouragement in this endeavor.

Conflict of interest

The authors declare no conflict of interest.

Source of funding

None.

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Table 1. Distribution of cases according to the age

Age in years	*n*	%
<20	26	8.6
21-25	180	60
26-30	82	27
31-35	12	4

Table 2. Relationship between placental location and PIH

Placental location	Outcome		Odds ratio	95% CI
	PIH	No PIH		
Lateral *n*= 168	112(66.6%)	56(33.3%)	5.09	(2.40-10.88)
Central *n*= 132	48(36.3%)	84(63.6%)		

X^2= 22.25, p = 0.00002

Table 3. Distribution of cases according to the severity of hypertension

Severity of hypertension based on DBP in (mm of Hg)	Number of cases, *n* = 160
Mild(90-99)	78
Moderate(100-109)	54
Severe(>110)	28

Table 4. Distribution of severity of PIH between different placental groups

Severity of Hypertension based on DBP	Centrally located Placenta	Laterally located Placenta
Mild(90-99)	32	46
Moderate(100-109)	14	40
Severe(>110)	2	26