

Placental Laterality as a Predictor for Development of Pre-Eclampsia

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ABSTRACT

BACKGROUND

Hypertensive disorders complicate 5 to 10 percent of all pregnancies; Pre-eclampsia syndrome, either alone or superimposed on chronic hypertension, is the most dangerous. 16% of maternal deaths were reported due to hypertensive disorders in developed countries according to WHO. The basic classification is of 4 types: - Gestational hypertension, pre-eclampsia and eclampsia syndrome, chronic hypertension, pre-eclampsia superimposed on chronic hypertension. Gestational hypertension- blood pressure of >140/90 mmHg without proteinuria, developing after 20 weeks of gestation in a previously normotensive woman. Pre-eclampsia is a multisystem disorder of unknown aetiology is characterised by blood pressure of >140/90 mmHg with proteinuria after 20 weeks of gestation in a previously normotensive and nonproteinuric woman. Eclampsia is pre-eclampsia complicated with grand mal seizures and/or coma. Chronic hypertension is known hypertension before pregnancy or hypertension diagnosed first time before 20 weeks of pregnancy.

METHODS

This is a prospective observational study carried out in the department of obstetrics and gynaecology of Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar. The study period was two years from January 2017 to March 2019. A total of 50 singleton pregnant women were included in the study to evaluate relationship between placental location and occurrence of pre-eclampsia and to find out whether placental laterality as determined by ultrasound can be used as a predictor of development of pre-eclampsia. To evaluate relationship between placental location and occurrence of pre-eclampsia, incidence of pre-eclampsia in patients with centrally and laterally located placenta was studied to find out as to whether placental laterality as determined by ultrasound can be used as a predictor of development of pre-eclampsia.

RESULTS

The incidence of pre-eclampsia was 14 in 50 singleton pregnancies. The maximum number of pre-eclampsia occurred between 21-25 years and was more common in primigravida (49%) than in second and multigravida. Out of 49% primigravida, 11% had lateral placenta and 38% had central placenta. Out of 11% lateral placenta 7% developed severe pre-eclampsia. Incidence of complications of pre-eclampsia like IUGR and low APGAR score were also more when pre-eclampsia has developed with a laterally implanted placenta compared to central placenta. All these show evidence of existence of significant association between placental laterality and presence of pre-eclampsia, intra uterine growth restriction or both.

CONCLUSIONS

Ultrasonography is simple, non-invasive, easy to perform, cost effective, diagnostic method to identify high risk cases. Females with laterally located placenta have a five times greater risk of developing pre-eclampsia. So, these pregnancies may require careful obstetric management to achieve a more favourable outcome and decrease the maternal and perinatal morbidity associated with pre-eclampsia

KEY WORDS

Placenta, Placental Laterality, Placental Position, Pre-Eclampsia, Ultrasound

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BACKGROUND

Hypertensive disorders complicate 5 to 10 percent of all pregnancies; and together they are one member of the deadly triad¹ along with haemorrhage and infection that contributes greatly to maternal morbidity and mortality. Pre-eclampsia syndrome, either alone or superimposed on chronic hypertension, is the most dangerous. 16% of maternal deaths were reported due to hypertensive disorders in developed countries according to WHO². Quality antenatal care, early diagnosis of hypertensive disorders and a high index of suspicion is the key to early diagnosis of complications and timely intervention. The basic classification is of 4 types:- Gestational hypertension- blood pressure of $>140/90$ mmHg without proteinuria, developing after 20 weeks of gestation in a previously normotensive women pre-eclampsia-Multisystem disorder of unknown aetiology characterised by blood pressure of $>140/90$ mmHg with proteinuria after 20 weeks of gestation in a previously normotensive and nonproteinuric woman eclampsia—women with pre-eclampsia complicated with grand mal seizures and/or coma chronic hypertension—known hypertension before pregnancy or hypertension diagnosed first time before 20 weeks of pregnancy pre-eclampsia superimposed on chronic hypertension. Pre-eclampsia is a complex clinical syndrome involving multiple organ systems and still remains the principal cause of maternal and perinatal mortality and morbidity.

HELLP syndrome: severe form of preeclampsia characterised by haemolysis, abnormal peripheral blood smear, bilirubin >1.2 mg/dl), thrombocytopenia ($<100,000/\text{mm}^3$) and elevated liver enzymes (AST >70 IU/L, LDH >600 U/L) Prediction of pre-eclampsia using clinical risk factors:- primiparity, previous pre eclamptic pregnancy, chronic hypertension, history of thrombophilia, multifetal pregnancy, invitro fertilization, family history of pre-eclampsia, type 1 diabetes or type 2 diabetes mellitus, obesity.³ Pathogenesis involves vasospasm, endothelial cell injury, increased pressor responses, prostaglandins, nitric oxide, endothelins, angiogenic and antiangiogenic proteins.^{4,5}

Measurement during early pregnancy-or across pregnancy- of various biological, biochemical and biophysical markers implicated in pre-eclampsia syndrome pathophysiology has been proposed to predict its development. Attempts have been made to identify early markers of faulty placentation, impaired placental perfusion, endothelial cell activation and dysfunction and these have resulted in testing activation of coagulation.⁶ For the most, strategies with poor sensitivity and with poor positive-predictive value for pre-eclampsia (Conde-Agudelo, 2014, Lindheimer, 2008b, Odibo, 2013).^{4,5,6} Currently, no screening tests are predictably reliable, valid, and economical (Kleinrouwefer, 2012) There are, however, combinations of tests, some yet to be adequately evaluated, that may be promising (Dugoff, 2013; 2011'Navaratnam, 2013; Olsen, 2012). A number of studies have shown that location of placenta may influence the uterine blood flow distribution and predispose the pregnancy to an adverse outcome like PIH. In the past two decades ultrasonography has proved to be the safest, easiest, and most accurate method for assessing placental laterality⁷ the non-invasive studies in second trimester of pregnancy revealed defective uterine perfusion

in laterally implanted placenta. Pre-eclampsia occurs only in the presence of chorionic villi. It has been shown that in humans both uterine arteries have a significant number of branches and that each supply the corresponding side of the uterus. Although that each supply the corresponding side of the uterus, anastomoses between the two uterine arteries exist, there is no proof that these are functional⁸. When the placenta is laterally located, the uterine artery closer to the placenta has lower resistance than the one opposite to it. In patients with centrally located placentas both uterine arteries demonstrated similar resistance¹. 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 cases the utero-placental blood flow needs are met primarily by one of the uterine arteries with same contribution from the other uterine artery via the collateral circulation.⁹ The degree of collateral circulation may not be the same in all patients and deficient contribution may facilitate the development of pre-eclampsia, intrauterine growth restriction or both the cytotrophoblasts fail to adopt a vascular adhesion phenotype in pre-eclampsia. This may explain the reduced trophoblastic invasion in laterally situated placenta when the uteroplacental blood flow needs are mainly met by one side uterine artery. Prediction of pre-eclampsia using clinical risk factors:-primiparity, previous pre eclamptic pregnancy, chronic hypertension, history of thrombophilia, multifetal pregnancy, invitro fertilization, family history of pre-eclampsia, type 1 diabetes or type2 diabetes mellitus, obesity.^{6,10}

We wanted to evaluate relationship between placental location an occurrence of pre-eclampsia, incidence of pre-eclampsia in patients with centrally and laterally located placenta, find out whether placental laterality determined by ultrasound can be used as a predictor of development of pre-eclampsia.¹¹

METHODS

The prospective observational study with the consent from the ethical clearance committee of Chalmeda Anand Rao institute of medical sciences, Karimnagar the study has been carried out in the department of obstetrics and gynaecology which is a prospective study. The study was carried out by taking the informed consent from the patient. The study period is two years from JANUARY 2017 TO MARCH 2019. A total of 50 singleton pregnant women is undertaken to evaluate relationship between placental location and occurrence of pre-eclampsia and to find out whether placental laterality as determined by ultrasound can be used as a predictor of development of pre-eclampsia.^{9,10}

Sampling Technique

Convenience sampling.

Diagnostic Criteria

Based on the location of placenta.

Inclusion Criteria

All primigravida and multigravida with singleton pregnancy. Diagnosis and classification of hypertensive disorders is

according to the criteria by the working group of national high blood pressure education programme (2000).¹² The location of placenta is determined around 18-24 weeks of gestational age, The placenta is classified as central when it is equally distributed between the right and left side of the uterus irrespective of anterior, posterior and fundal position. When 75% or more of the placental mass is to one side of the midline, it is classified as unilateral right or left placenta.^{8,7}

Exclusion Criteria

Multiple gestation, chronic hypertensive patients, renal diseases, uterine anomalies, diabetes previous history of pre-eclampsia and eclampsia history of smoking IUD, documented major congenital anomalies, collagen vascular diseases, patients who are not willing for follow up.

Statistical Tool

SPSS Software.

RESULTS

Out of 50 patients who were included in this study 13 had lateral placenta and 37 had central placenta—Distribution of cases according to development of pre-eclampsia Incidence of pre-eclampsia is around 7%.¹³

Distribution of Cases According to Parity

Out of 50 patients 30% were primi, 13% were second gravida and 7% were multi gravida.

Distribution of Cases According to Age

Out of 50 patients 5 were of age 20 and <20, 26 were around 21-25 years, 15 were of age 26-30 years, 4 were of 31-35 years of age.

	Primigravida	Second	Multi
Lateral	6	4	4
Central	19	14	3

Table 1. Relation between Parity and Location Placenta

Parity	Mild Pre-Eclampsia	Severe Pre-Eclampsia
Primi gravid	3(33.3)	6(66.6)
Second gravid	2(66.6)	1(33.3)
Multi gravid	1(50%)	1(50%)

Table 2. Relation between Parity and Severity of Preeclampsia

APGAR (4-6)	APGAR (6-8)	APGAR (8-10)
2(14.3%)	5(35.7%)	7(50.0%)

Table 3. Neonatal Outcome Based on APGAR Scores in Patients with Lateral Placenta

APGAR (4.6)	APGAR (6-8)	APGAR (8-10)
1(2.8%)	5(13.9%)	30(83.3)

Table 4. Neonatal Outcome Based on Apgar Score in Patients with Central Placenta

Mode of Delivery	Primi	Second	Multi
Vaginal	2(14.3)	1(7.1)	3(21.4)
Caesarean	4(28.6)	3(21.4)	1(7.21)

Table 5. Analysis of Mode of Delivery in Patients with Central Placenta

Mode of Delivery	Primi	Second	Multi
Vaginal	11(31.5)	11(31.5)	3(8.2)
Caesarean	7(20.5)	3(8.2)	0(0)

Table 6. Mode of Delivery in Patients with Central Placenta

Position of Placenta	Primigravida ¹⁰	Second Gravida ⁴	Multigravida ¹²
Central	2(22.22%)	1(33.33)	0(0%)
Lateral	7(77.78%)	2(66.67%)	2(100%)
Total	9(64.28%)	3(21.42%)	2(14.28%)

Table 7. Relation between Parity, Location of Placenta

Primigravida 2(66.66%)		Second Gravida 1(33.33%)	
Central placenta	Lateral placenta	Central placenta	Lateral placenta
0	2(100%)	0	1(100%)

Table 8. Relation between Parity, Location of Placenta and Complication of Pre-Eclampsia like IUGR

Out of 36 patients with central placenta, 26(71%) patients delivered by vaginal route 10(29%) patients underwent caesarean section.

DISCUSSION

Pre-eclampsia is a complex clinical syndrome involving multiple organ systems and still remains the principal cause of maternal and perinatal mortality and morbidity. The search for an ideal predictive and preventive measure remains challenging.¹⁴ The source of blood supply for the placenta are the two uterine arteries there is poor evidence of efficient functional collateral anastomosis between the two uterine vessels, so in a centrally located placenta, the blood flow will be abundant from both uterine arteries, but a laterally implanted placenta (Which is diagnosed if 75% or more is to one side of the uterine cavity) gets its blood supply from one uterine artery which is insufficient for adequate placental perfusion this causes predisposition to uteroplacental insufficiency and IUGR. A deficient perfusion of the placenta will impede proper trophoblastic invasion of spiral arterioles which is primary inciting factor in development of pre-eclampsia.¹⁵ The present study shows increased incidence of pre-eclampsia, intra uterine growth restriction and relatively poorer neonatal outcome in patients with lateral placenta which is statistically significant and correlates well with previous studies.¹¹

The pathophysiological characteristics of pre-eclampsia are complex, and the cause remains unknown. One of the fundamentals disturbances in patients with this condition is decreased uteroplacental blood flow. However, whether this is the cause or result yet to be discussed. Our data indicate that the presence of lateral is strongly associated with preeclampsia. The present study shows that the location of placenta in primigravidae, second gravidae and multi gravidae may predict the development of pre-eclampsia, IUGR and its complications to a considerable extent and may be used as simple, non-expensive, easily accessible and reproducible screening test for the prediction of pre-eclampsia and IUGR.¹⁶ Further studies are necessary to evaluate the sensitivity of placental laterality is a predictor of the development of pre-eclampsia. As yet there is no practical, acceptable and reliable screening test for pre-eclampsia that has been thoroughly tried and tested. In the present study placental laterality has a sensitivity of 78.57% which though low is much better than most other tests. Besides, it has a very good specificity of 81.39% and negative predictive value of 95.89%. Its positive predictive value is low but so is the case with most other tests. It is a very useful

cost effective and easy to perform non-invasive test. Present study correlates well with the study conducted by Dr. Muralidhar Pai and the study conducted by Dr. Kofinas. Incidence of lateral placenta is around 13% in the present study out of 50 patients which correlates well with the studies of Pai MV Pillai J et al 2005, Bhalerao AV et al 2013, Rajeshwari Pillay et al. Out of 50 patients 7 patients developed pre-eclampsia this is comparable with SJ Kore et al 2016, Pai MV Pillai J et al 2005, Bhalerao AV et al 2013, Preety et al, Chinnappa et al, Parul S Jani et al. In present study out of 13 patients with lateral placenta, 7 patients developed pre-eclampsia. Incidence is around 14% which is comparable with the previous studies Preveena Fareed et al, Bhalerao AV et al 2013, Patel A et al 2012, Parul S Jani et al. Present study out of 50, 37 patients had central placenta, well comparable to previous studies PAI MV PILLAI J et al 2005, Bhalerao AV et al 2013, Rajeshwari Pillay et al 2015. Present study out of 37 patients with central placenta 3 patients developed pre-eclampsia incidence is 4.1% which is comparable with previous studies PAI MV PILLAI J et al 2005, Bhalerao AV et al 2013, Preety et al, Chinnappa et al.

CONCLUSIONS

In case of unilateral placenta, the absence or insufficient trophoblastic invasion of arteries on contralateral side would make them retain their sensitivity to vasoactive substance during pregnancy. 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 18-24 weeks is associated with increased risk of development of pre-eclampsia. Females with laterally located placenta have a five times greater risk of developing pre-eclampsia so these pregnancies may require careful obstetric management to achieve a more favourable outcome and decrease the maternal and perinatal morbidity associated with pre-eclampsia.

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