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Original Research Article

Prospective cohort study in relation of placental location and risk of developing preeclampsia in a tertiary care hospital

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ABSTRACT

Background: Preeclampsia is one of the leading and unpredictable causes of maternal morbidity and mortality. This study was done to find the association between location of placenta and the development of preeclampsia as well as its correlation with severity of preeclampsia.
Methods: This prospective cohort study was conducted in government medical college hospital, Pudukottai, Tamil Nadu, India between March 2021 to December 2021. The 150 pregnant women were registered in this study. The location of the placenta was determined by ultrasound at 18-24 weeks. The placenta was classified as central and lateral. The endpoint of the study was the development of hypertension or delivery.
Results: The incidence of preeclampsia was 32%. Primigravida was a significant high-risk factor. Preeclampsia was more common in 20-25 years (52.1%). Among 48 women who developed preeclampsia, 32 had lateral location of placenta and 16 had central location of placenta. Lateral location of placenta in predicting preeclampsia, $p<0.0001$, which is clinically significant. Lateral location of placenta has high incidence of both severe 66.7% and non-severe preeclampsia 67.6%. The sensitivity-66.6%, specificity-78.4%, positive predictive value-59.2%, negative predictive value-83.3% and the likelihood ratio of 3.09 of our study are significant.
Conclusions: This study shows that placental location determined by ultrasonogram between 18-24 weeks of gestation is an excellent screening tool for the prediction of pre-eclampsia. Lateral placentation helps to identify who are at greatest risk and those requiring careful obstetric management to achieve a more favourable outcome and to decrease the maternal and perinatal morbidity and mortality with preeclampsia.

Keywords: Preeclampsia, Placental laterality, Central placenta

INTRODUCTION

Hypertensive disorders complicate 5-10% of all pregnancies and together they are one of the deadly triads that contribute greatly to maternal morbidity and mortality rates.[1] Of hypertensive disorders, the preeclampsia syndrome, either alone or superimposed on chronic hypertension is the most dangerous.[1] Preeclampsia is a complex clinical syndrome involving multiple organ systems and still remains the principal cause of maternal and perinatal mortality and morbidity. Incidence of pre-eclampsia is commonly cited to be about 5%.[1,2] Preeclampsia occurs only in the presence of placenta. Incidence is influenced by parity, race and genetic factors.[4,5] According to WHO, in developed countries, 16% of maternal deaths were attributed to hypertensive disorders.[1] Maternal mortality due to hypertensive disorders in India ranges from 2-30%.[6,7]

FOGSI and other studies shows incidence of preeclampsia in India ranges 11-13%.[8] Preeclampsia is a multiorgan disease process of unknown aetiology characterised by de novo development of hypertension and proteinuria after 20 weeks of gestation. It is a pregnancy specific syndrome that can affect virtually any organ system.

Conventional mercury sphygmomanometer is the gold standard for blood pressure measurement.[9] A fetus is not a requisite for preeclampsia to develop. And although chorionic villi are essential, they need not be intrauterine, as preeclampsia can develop with an abdominal pregnancy by Worley et al.[10] The concept of vasospasm with preeclampsia has been advanced for a century by Volhard.[11] Various biological markers implicated in the preeclampsia syndrome have been measured to help in preventing its development. A number of mechanisms have been proposed to explain the cause of preeclampsia, among which placental implantation with abnormal trophoblastic invasion of uterine vessels is currently considered important. The search for an ideal predictive test and preventive measure remains challenging.

Among the various predictors for preeclampsia, the placental location by ultrasound at 18-24 weeks is very cost-effective, non-invasive and has a good positive predictive value.[12] It is possible that when the placenta is centrally located, the uteroplacental blood flow needs are met by equal contribution from both the 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 side via collaterals. In the women with centrally located placenta, both uterine arteries demonstrate similar resistance.[13,15] In laterally located placenta, the uterine artery close to the placenta has lower resistance than the one opposite from it and the uteroplacental blood flow needs to be met primarily by one of the uterine arteries with some contribution by the other uterine artery via collateral circulation.[13,14] The degree of collateral circulation may not be the same in all women and deficient contribution facilitates the development of preeclampsia.[16] Screening the population in search for disease at its earlier stages, is a logical extension in the role of preventive medicine. If we wish to prevent such disorder, we must seek ways of preventing or ameliorating the disease process. In preventing this disorder, the most important factor is lack of timely prediction. Various biological markers implicated in the preeclampsia syndrome have been measured to help predict its development. Although most have been evaluated in the first half of pregnancy, some have been tested as predictors of severity in the third trimester according to Mosimann et al.[17] The ability to predict those women at risk for preeclampsia in very early pregnancy might decrease maternal and fetal morbidity through closer surveillance and early intervention. Determination of placental position by ultrasonogram at 18-24 weeks is also a highly sensitive test for prediction of preeclampsia by Kofinas et al.[18]

Aim of the study

The aim was to study relationship between the placental location determined by ultrasonogram at 18-24 weeks and development of preeclampsia and severity of preeclampsia.

METHODS

This Prospective cohort study was conducted between March 2021 and November 2021 at the department of obstetrics and gynaecology, government medical college, Pudukottai, Tamil Nadu, India. The 150 pregnant women attending the antenatal clinic at government medical college, Pudukottai were registered in this study. Inclusion criteria were Singleton pregnancy, gestational age between 18-24 weeks and those patients who are willing for follow up. Exclusion criteria were gestational age <18 and >24 weeks, multiple pregnancy, uterine anomalies, chronic hypertension, diabetes mellitus, renal disease, severe anaemia, thyrotoxicosis, Rh-incompatibility, connective tissue disorder and positive lupus anticoagulant.

A written informed consent was obtained from all the pregnant women included in the study. No dietary alterations were recommended. Detailed history was taken. Complete examination was done which included general examination, clinical examination of cardiovascular system, respiratory system, central nervous system and obstetric examination. Blood pressure was recorded in sitting posture and phase Korotkoff V sound was taken to determine the diastolic component. Basic investigations of haemoglobin, blood grouping and Rh typing, platelet count, blood urea, serum creatinine, SGOT, SGPT and urine-albumin were done. The location of the placenta was determined by ultrasound at 18-24 weeks in all 150 women. The placenta was classified as central when it was equally distributed between the right and the left side of the uterus irrespective of anterior, posterior or fundal position. When 75%/ more of the placental mass was to one side of midline, it was classified as unilateral right or left placenta. The endpoint of study was the development of hypertension as per ACOG criteria or delivery. Followed up with routine antenatal visits for signs, symptoms of pre-eclampsia by routine examination of blood pressure, serial weight and investigation of pre-eclampsia when required and results were tabulated.

The outcome has been analysed with respect to age, parity, placental location, severe and non-severe preeclampsia, Incidence of HELLP syndrome and severity of proteinuria. Data were entered in the excel spread sheet and variables were coded accordingly. The statistical analyses were performed using Graph pad Prism version 5 software. Data were presented as frequency with proportion n (%) for categorical. Fisher's exact test (for sample<30) was used to compare the proportions between groups as appropriate. $P<0.05$ was considered statistically significant.

RESULTS

Preeclampsia is more common in the age group of 20-25 years with a frequency of 52.1% and primigravida was found to be a significant high-risk factor with the incidence of preeclampsia in our study is 32% (Table 1). Central location of placenta was more common in 96 (64%) patients whereas lateral location in 54 patients (Table 2).

Both central and lateral location of placenta is more common in 20-25 year (Table 3). No significant differences in incidence of placental location in relation to gravida (Table 4). Among the 48 women who developed preeclampsia, 32 women had lateral location of placenta and 16 women had central location of placenta (Table 5). In our study, lateral location of placenta in predicting preeclampsia, p<0.0001, which is clinically significant. The relative risk with 95% CI in our study shows that women with lateral location of placenta have 3.5 times more the risk of developing preeclampsia than women with central location of placenta (Table 6). Women with lateral location of placenta had high incidence of both severe (66.7%) and non-severe preeclampsia (67.6%) and among 48 cases, 13 (27.1%) developed imminent symptoms (Table 7). The incidence of HELLP syndrome in study was 10.8% (Table 8). Statistically, significance difference was noted in development of preeclampsia in laterally located placenta (Table 9). Sensitivity-66.6%, specificity-78.4%, PPV-59.2%, NPV-83.3% and likelihood ratio of 3.09 of study are the significant (Table 10).

Table 1: Distribution of age and gravida.

Age (Years)	Study population		Preeclampsia		Gravida	Study population		Preeclampsia	
	N	%	N	%		N	%	N	%
<20	12	8	7	14.6	Primi	51	34	17	35.4
20-25	91	60.6	25	52.1	Gravida 2	24	32	13	27.1
26-30	37	24.7	12	25	Gravida 3	25	34	18	37.5
>30	10	6.7	4	8.3					
Total	150	100	48	32	Total	150	100	48	100

Majority were in the age group of 20-25years and most are primi and third gravida, incidence of preeclampsia was 32%

Table 2: Type of placental location, (n=150).

Type of placental location overall	N	Percentage (%)
Central location	96	64
Lateral location	54	36
Total	150	100

The 96 (64%) had central location of placenta and 54 (36%) had lateral location of placenta.

Table 3: Type of placental location with respect to age.

Age (Years)	Central location, (n=96)		Lateral location, (n=54)	
	N	%	N	%
<20	4	4.2	8	14.8
20-25	68	70.8*	23	42.6*
26-30	23	23.96	14	25.9
>30	1	1.04	9	16.7
Total	96	100	54	100

The incidence of central and lateral location of placenta was higher among 20-25 years.

Table 4: Type of placental location with respect to gravida.

Gravida	Central location, (n=96)		Lateral location, (n=54)	
	N	%	N	%
Primigravida	29	30.2	22	40.7
Gravida 2	34	35.4	14	26
Gravida 3	33	34.4	18	33.3
Total	96	100	54	100

Fisher's exact test was used. There was no significant difference (p=0.514).

Table 5: Comparison of risk of developing preeclampsia with gravida.

Gravida	Patient developed preeclampsia, (n=48)		Patient not developed preeclampsia, (n=102)	
	N	%	N	%
Primigravida	17	35.4	34	33.3
Gravida 2	13	27.1	35	34.3
Gravida 3	18	37.5	33	32.4
Total	48	100	102	100

Fisher's exact test was used and no significant difference was noted (p=0.66).

Table 6: Relationship between the placental location and development of preeclampsia.

Variables	Patient developed preeclampsia (n=48)	Patient not developed preeclampsia, (n=102)	P value	Relative risk with 95% CI
Lateral location of placenta, (n=54)	32	22	<0.0001*	3.5 (2.1 to 5.8)
Central location of placenta, (n=96)	16	80		

Women with lateral location of placenta was significantly associated with the development of preeclampsia. *indicates p<0.05 and considered statistically significant. CI=Confidence interval. The p<0.0001 which is statistically significant. Relative risk with 95% CI shows that women with lateral location of placenta have 3.5 times the risk of developing preeclampsia.

Table 7: Comparison of severity of preeclampsia and development of imminent symptoms with type of placental location.

Location of placenta	Severe preeclampsia		Non-severe preeclampsia		Developed imminent symptoms		Not developed imminent symptoms	
	N	%	N	%	N	%	N	%
Lateral location	9	64.3	23	67.6	8	61.5	24	68.6
Central location	5	35.7	11	32.4	5	38.5	11	31.4
Total	14	29.1	34	70.9	13	27.1	35	72.9

Severe preeclampsia was more common in lateral location. Fisher's exact test was used and no significant difference was noted (p=0.82).

Table 8: Abnormal parameters in preeclampsia.

Abnormal parameters in preeclampsia	N	Percentages (%)
Thrombocytopenia (count <1 L/cc)	4	8.3
Increased liver enzymes- HELLP*syndrome	5	10.4
Elevated renal parameters	0	0
Urine albumin		
4+	3	6.25
3+	7	14.58
2+	20	41.66
1+	8	16.66

*HELLP-Haemolysis, elevated liver enzymes, low platelets

Table 9: The predictive factors of location of placenta for development of preeclampsia.

Variables	Patient developed preeclampsia, (n=48)	Patient not developed preeclampsia, (n=102)	P value	Relative risk with 95% CI
Lateral location of placenta, (n=54)	32	22	<0.0001*	3.5 (2.1 to 5.8)
Central location of placenta, (n=96)	16	80		

Table 10: Predictive factors derived from the above 2×2 contingency table.

Parameters	Statistics (%)	95% Confidence interval
Sensitivity	66.6	0.51 to 0.79
Specificity	78.4	0.69 to 0.85
Positive predictive value	59.2	0.45 to 0.72
Negative predictive value	83.3	0.74 to 0.9
Likelihood ratio	3.09	---

Thus, women with lateral location of placenta have 3.09 times the likelihood of developing preeclampsia compared with women with central location of placenta.

DISCUSSION

In this study, 150 patients were registered. Of the 150 patients, 48 developed preeclampsia with an incidence of 32% and is comparable with studies done by Sumathi et al and Chandra et al with the incidence of 48% and 52% respectively.[19,20] Women of different age group were included in the study group. The 60.7% were in the age

group of 20-25 years. Central as well as lateral location of placenta was also common in the age group of 20-25 years and this makes our study comparable with Kofinas et al whose mean maternal age with both central and lateral location of placenta was 23.9 with a p=1.00.[18] Among the women who developed preeclampsia, 52.1% were in the age group of 20-25 years. In the study by Chandra et al the majority of patients were in the age group of 21-25 years and the incidence of central and lateral location of placenta was common in the age group of 21-25 years.[20]

Age distribution of women who developed preeclampsia and in our study women of 20-25 years were more prone to develop preeclampsia (n=25) with a frequency of 52.1%. It is comparable to the study done by Kore SJ et al where the frequency of preeclampsia among women in the age group of 21-25 years was 41%.[21] In our study, 34% were primi-gravidas and 66% were multigravidas which is comparable to 37.55% in primigravida, 62.45% in multigravida in study by Pai Muralidhar et al and Kore et al study reported as primigravida-34.5%, multigravida-65.5%.[22,21]

The distribution of type of placenta in the study population shows 64% of women had central location of placenta and 36% of women had lateral location of placenta. In our study, development of preeclampsia in lateral placental location was 66.66% with p<0.0001which is statistically significant. Relative risk with 95% CI shows that women with lateral location of placenta have 3.5 times the risk of developing preeclampsia. It is comparable to 74% with p<0.03 in Kofinas et al study, 81.7% with p<0.001 in Sumathi et al study, 74% with p<0.0001 in Pai Muralidhar et al study and 59.38% with p<0.001 in Kore et al study.[18,19,22, 21]

Out of the 48 women who developed preeclampsia in the study group, 70.9% developed non-severe preeclampsia and 29.1% developed severe preeclampsia. In our study, both severe (66.7%) as well as non-severe preeclampsia (67.6%) was common among women with lateral location of placenta. It is comparable to development of non-severe preeclampsia in 69.3% in Sumathi et al study and 52% in Chandra et al study and development of severe preeclampsia in 91.8% in Sumathi et al and 76.9% in Chandra et al study.[19,20] Among the 48 women who developed preeclampsia, 27.1% (n=13), presented with imminent symptoms. In our study, 20.8% of women with severe preeclampsia presented with proteinuria. 10.8% of women presented with HELLP syndrome, which is comparatively higher with the incidence of 2.5% in the study by Sumathi et al.[19.] Comparison of predictive value of placental laterality in present study with other studies women with lateral location of placenta has 3.09 times the likelihood of developing preeclampsia compared with women with central location of placenta. Our study had a sensitivity of 66.6% which was comparable with 59.38% in study by Kore et al 73% in Pai Muralidhar et al 66.6% in Kakkar, Sandhya et al study study.[21-24] The specificity of our study was 78.4% which correlates well with 76.67% in study done by Sumathi et al.[19] The positive predictive value of our study was 59.2% which was higher when compared to 35.54% in study by Sumathi et al 46% in Kofinas et al study and correlated well with 51% in Pai Muralidhar et al study.[19,18,22] The negative predictive value of our study is 83.3% which correlates well with the studies done by Sumathi et al (88.05%) and Kofinas et al (90%).[19,18] Thus, placental position is an easy non-invasive test to predict preeclampsia.

When placenta is laterally located, in the majority of the cases, the uteroplacental blood flow needs are met primarily by one of the uterine arteries with some contribution from the other uterine artery via collateral circulation. The degree of collateral circulation may not be same in all women and deficient contribution may facilitate the development of preeclampsia. This is the limitation of this prediction test.

CONCLUSION

The study shows that placental location determined by ultrasonogram between 18-24 weeks of gestation is an excellent screening tool for the prediction of preeclampsia among numerous screening test. This test is ideal because it is simple, easy to perform, inexpensive, part of the anomalies scan performed, non-invasive and convenient for the patient. Lateral placentation helps to identify the population who is at greatest risk and those requiring careful obstetric management to achieve a more favourable outcome and to decrease the maternal and perinatal morbidity and mortality associated with preeclampsia.

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