Original Article

DOI: 10.17354/ijss/2015/362

Morphological Changes of Placenta in Cases of Pre-eclampsia and Perinatal Outcome

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Abstract

Background: Hypertensive disorder of pregnancy is most common medical problem complicating 3-8% of pregnancies. As pathophysiology lies in placenta most attention is drawn on placenta. In recent years it acts as valuable indicator for maternal and fetal diseases.

Objectives: The objective of study was to assess the morphological changes of placenta and to correlate the findings with severity of disease and with fetal outcome.

Materials and Methods: Total of 400 placentae of which 200 placentae from cases of pre-eclampsia (PE) (100-mild, 100-severe) and 200 placentae from normal cases were studied in labor room Vijayanagara Institute Medical Sciences, Bellary. The morphometric parameters of placenta like weight, volume, thickness, diameter, shape, number of cotyledons were recorded. Gross features like infarctions, calcifications, retro placental (RP) hematoma were noted and fetal parameters like fetal weight and Apgar score at 1st and 5th min recorded.

Results: There was a significant correlation between placental weight and weight of baby and neonatal intensive care unit admission $P < 0.001$. Placental morphometric features like mean weight, volume, thickness, diameter, number of cotyledons values were significantly less in severe PE group compared to mild PE group with $P < 0.001$ and compared to control group all parameters are significantly less in study group ($P < 0.001$). There was significant correlation between infarction and fetal birth weight ($P < 0.001$). There were 5 still births 4 in severe PE and 1 in mild PE. The placentae of this still birth were having calcifications, infarctions and RP clots. Mean fetoplacental (F/P) ratio was higher in study group compared to control group ($P < 0.001$).

Conclusion: In present study the placental morphometric features like placental weight, volume, diameter, thickness were low with increasing grades of hypertension compared to control group. There was an increased F/P weight ratio in the hypertensive group. The study of morphological changes of placenta in cases of PE may help us to plan the treatment plan for better outcome of mother and newborn. Serves as important medico legal record.

Key words: Apgar score, Morphology, Placenta, Perinatal outcome, Pre-eclampsia

INTRODUCTION

Placenta is discoid, haemochorial and a decidual structure developed during pregnancy and is the organ of exchange between the fetus and mother for the purpose of physiological exchange. It is considered as the accurate record of prenatal experiences. Hypertensive disorder of pregnancy along with hemorrhage and infection form one of the deadly triad that greatly contributes to maternal mortality and morbidity. Pre-eclampsia (PE) has been described as the disease of theories. One of the leading theories is that there is a maternal immunological response to the fetal immune system, resulting in abnormal transformation of the spiral arteries these leads to a high-resistance blood flow to the placenta. The turbulence of the blood flow and hypoxia in the placenta then give rise to a destruction of placental tissue and release of factors, such as soluble vascular endothelial growth factor receptor-1,

Access this article online

www.ijss-sn.com

Month of Submission : 07-0000
Month of Peer Review : 07-0000
Month of Acceptance : 07-0000
Month of Publishing : 08-0000

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syncytio-trophoblast membrane micro particles, fetal RNA and DNA, which might injure maternal endothelium and be responsible for the maternal symptoms in PE.[1-6] In addition it has its effect on fetal growth restriction, prematurity, contributing largely to perinatal mortality and morbidity. Morphologically placentae of hypertensive disorders of pregnancy are lighter in weight, lesser in diameter and thickness. Abnormal shape, cord insertion and with diminished fetoplacental (F/P) ratio. There is higher incidence of infarction, retro placental (RP) hematoma, sub-chorionic fibrin. These placental changes are directly proportional to the duration of the disease and its severity. Decrease of fetal weight is significantly larger than placental weight loss. Most obstetricians and pediatricians would agree that the examination of placenta often helps to explain an abnormal neonatal outcome. As in our country still many unbooked patients visit the hospital only for delivery, it may be possible to decide whether the pathological condition that endangered the well-being of the fetus was an acute or a chronic process. Conditions with the risk of recurrence can be recognized, resulting in counseling and management of subsequent pregnancies. Despite the understanding and appreciation of placental disease, great resistance still exists in performing placental examination routinely. So the detail study of placentae morphologically done in cases of PE to know significant changes compared to normal and its fetal outcome.

MATERIALS AND METHODS

After taking ethical clearance from the institute study of a total of 200 placentae from cases of PE (100-mild, 100-severe) and 200 placentae from normal cases attending the Vijayanagara Institute Medical Sciences, Obstetrics and Gynecology Bellary, Labor room were studied from December 2011 to September 2013.

Inclusion Criteria

All pregnant women admitting to the labor room with gestational age >34 weeks irrespective of age and parity were included.

Exclusion Criteria

Twin pregnancy, Rh negative pregnancy, pregnancy with - gestational diabetes, heart diseases, autoimmune disorders, chronic hypertension; placenta previa and eclampsia were excluded.

Samples were grouped into three groups as Group A, Group B, Group C.

Group A: This group comprised of pregnant women with mild PE.
Group B: This group comprised of pregnant women with severe PE.
Group C: This group comprised of pregnant women without PE.

The criteria adopted for grouping of the cases were defined according to the Working Group of National High Blood Pressure Education Programme (2000).

Detailed obstetric and medical history was taken for all cases, clinical examination done and they were subjected to following investigations:

1. Urine: Sugar, albumin, microscopy
2. Blood: Hemoglobin%, blood grouping and Rh typing, HIV, hepatitis B surface antigen. Blood urea and uric acid, serum creatinine
3. Platelet count liver enzymes, fundoscopy.

Just after delivery all the placentae were collected in a clean tray. The membranes and cord at their attachment to the placenta was cut off. The placenta was gently expressed so as to remove its blood content and mopped with dry cotton pad. The following parameters of placenta were used for comparison among various study groups. Weight measured by weighing machine, with help of graduated metallic scale mean of two maximum diameters taken at right angles. Thickness measured by using thick needle which was inserted at 5 points and volume by water displacement method. Gentle pressure was put on the fetal surface to make the cotyledons prominent and cotyledons counted. RP hematoma, infarction, calcification. All parameters were measured using methods same as study done by Kishwara *et al*.[7] At the time of delivery fetal conditions like birth weight, Apgar score at 1 min and 5 min were noted. Babies admitted to neonatal intensive care unit (NICU) were followed up. F/P ratio calculated.

Statistical Analysis

Comparison of various parameters between study groups will be analyzed by ANOVA and by Student's test. Categorical data will be analyzed by Chi-square test.

RESULTS

Highest study subjects were from age group 21 to 30 years (64.5%) followed by <20 years (32.8%). Out of 400 study subjects 245 (61.3%) were primigravida and 155 (38.8%) were multigravida. 300 (75%) had spontaneous

vaginal delivery, 20 (5%) had induced vaginal delivery and 80 (20%) delivered by caesarean section. In the present study more number of preterm delivered cases belonged to the hypertensive group. Pre-term delivery 19 (9.5%) in normal cases, 11 (11.1%) mild PE, 20 (20.8%) severe PE. Most common shape of the placenta in our study was circular in both cases and controls about (90.2%). In severe PE the occurrence was 81 (91.0%) in mild PE it was 91 (91.0%). Compared to controls we observed more oval shaped placenta in cases. In severe PE 19 (19.0%), mild PE 7 (7.0%) and in controls 9 (4.5%) the findings were statistically significant ($P < 0.001$). Among both cases and controls central cord insertion was observed most commonly (95.0%). Compared to controls (2.5%) we observed more number of eccentric and marginal cord insertion in mild PE 8 (8%) and severe PE 7 (7%) $P < 0.068$.

We observed more calcification in severe PE group 35 (35.0%) compared to mild PE 13 (13.0%) and controls 5 (5.0%). This observed finding of increased incidence of calcification in severe PE compared to mild PE was significant $P < 0.001$. There was increased incidence of infraction in severe PE group 48 (48.0%), compared to mild PE 25 (25.0%) and controls 5 (2.5%). There was increased incidence of infraction in cases compared to controls 5 (2.5%). This observation of increased incidence of infraction in severe PE compared to mild PE and increased incidence of infarction in cases compared to controls was statistically significant $P < 0.001$ (S). Among study subjects number of cotyledons observed commonly between 16 and 20. We observed in severe PE group about 37% patients had 10-15 cotyledons compared to mild PE 25% and controls 11%. This observation is statistically significant.

As shown in Table 1 morphometric features of placenta like its weight, volume, thickness, diameter values are less in severe PE compared to mild PE and controls from this observation it was observed that morphometric features of placenta highly correlate with the severity of the disease.

Table 1: Placental morphometric study

Placental parameters	Mean±SD		
	Mild PE	Severe PE	Controls
	Group B	Group C	Group A
Weight	399.10±79.112	371.70±85.316	478.80±292.122
Volume	275.80±86.459	238.20±93.197	420.45±140.816
Thickness	1.96±0.197	1.77±0.423	2.02±0.199
Diameter	18.64±1.812	17.94±1.963	20.33±1.446
F/P ratio	6.15±0.757	6.40±0.888	5.89±0.769

P<0.001 (S). SD: Standard deviation, F/P: Fetoplacental, PE: Pre-eclampsia

Findings were statistically significant. F/P ratio increases as the severity of the disease increases.

There were 200 cases in hypertensive group and 200 normal cases. There were 5 still births in total study group and 4 still births in severe PE group, remaining 1 in mild PE group and there were no still births in control groups. These still births are excluded from the cross tabulations and the morphologic changes in placenta of still born babies are explained in respective discussion of each variables. In the study group the incidence of low Apgar was more compared to controls. In the study group incidence of still birth was more when placental weight 200-300 g with $P < 0.001$. Significant relation was noted between placental weight and neonatal death and NICU admission in study group. In the control group, incidence of low birth weight, stillbirth, neonatal death and NICU admission was more when placenta weighed between 200 and 300 g. There was significant correlation between infarction and fetal birth weight <0.001. These observations can be seen in Tables 2 and 3.

DISCUSSION

Placenta is a vital organ maintaining pregnancy and promoting fetal development, which functions as fount upon which developing fetus derives its nutritional substance and obtains its metabolic and immunological requirements. Gross placental measures can best assess the time of onset and cumulative placental effects of a suboptimal intrauterine environment. Maternal morbidity remains great with PE, which continues to be one of the leading causes for the admission of pregnant women to intensive care units. Furthermore, fetal mortality and morbidity is considerable, related to the effects of the disease on the fetus as well as prematurity. In present study morphometric parameters of placenta like, weight, volume were significantly reduced in pre-eclamptic group as compared to normal group ($P < 0.01$). This study had similarities to the study conducted by Majumdar *et al*.[8] and Virupaxi *et al*.[9] The placentae of PE patients were significantly smaller in diameter than the normal. The absolute volume of placenta was significantly lowered in the pre-eclamptic group than the control group.[10] It has also been reported by Nazmeen (2006) that weight and volume of the placenta was less in PE cases. As severity of hypertension increases, placental mean volume, diameter, thickness decreases this finding correlates with our study and study of Udainia and Jain,[11] Majumdar *et al*. Londhe and Mane.[12] We observed mean fetal weight of 2.24 g in severe PE 2.49 g in mild PE and 2.64 g in

Table 2: Comparison of placental weight

Placenta	Cases						
	Birth weight (%)		APS 1 (%)		APS 5 (%)		NICU
	<2.5 kg	>2.5 kg	<7	>7	<7	>7	Yes
Placental weight							
200-300 (44)	41 (93.2)	3 (6.8)	14 (31.8)	30 (68.2)	5 (11.4)	39 (88.6)	21 (47.7)
301-400 (89)	84 (94.4)	5 (5.6)	23 (25.8)	66 (74.2)	10 (11.2)	79 (88.8)	23 (25.8)
401-500 (58)	22 (37.9)	36 (62.1)	9 (15.5)	49 (84.5)	1 (1.7)	57 (98.3)	7 (12.1)
>500 (4)	0	4 (100)	0	4 (100)	0	4 (100)	0
	P=0.001		*P*=0.155		*P*=0.154		*P*=0.001
Calcifications							
Present (44)	39 (88.6)	5 (11.4)	15 (34.1)	29 (65.9)	6 (13.6)	38 (86.4)	20 (45.5)
Absent (151)	108 (71.5)	43 (28.5)	31 (20.5)	120 (79.5)	10 (6.6)	141 (93.4)	31 (20.5)
	P=0.020		*P*=0.062		*P*=0.136		*P*=0.02
Infarction							
Present (69)	62 (89.9)	7 (10.1)	20 (29.0)	49 (71.0)	6 (8.7)	63 (91.3)	21 (30.4)
Absent (126)	85 (67.5)	41 (32.5)	26 (20.6)	100 (79.4)	10 (7.9)	116 (92.1)	30 (23.8)
	P=0.001		*P*=0.189		*P*=0.853		*P*=0.314
Haematoma							
Present (27)	25 (92.6)	2 (7.4)	10 (37.0)	17 (63.0)	2 (7.4)	25 (92.6)	11 (40.7)
Absent (168)	122 (72.6)	46 (27.4)	36 (21.4)	132 (78.6)	14 (8.3)	154 (91.7)	40 (23.8)
	P=0.025		*P*=0.076		*P*=0.871		*P*=0.63

APS: Antiphospholipid syndrome, NICU: Neonatal intensive care unit

Table 3: Birth weight and NICU Admission

Placenta	Controls (%)						
	Birth weight		APS 1		APS 5		NICU
	<2.5	>2.5	<7	>7	<7	>7	Yes
Placental weight							
200-300 (10)	9 (90)	1 (10)	4 (40)	6 (60.0)	3 (30)	7 (70.0)	3 (30)
301-400 (49)	42 (85.7)	7 (14.3)	9 (18.4)	40 (81.6)	2 (4.1)	47 (95.9)	1 (2)
401-500 (115)	50 (43.5)	65 (56)	8 (7.0)	107 (93)	1 (0.9)	114 (99)	0
>500 (26)	0	26 (100)	1 (3.8)	25 (96.2)	0	26 (100)	0
	P=0.001		*P*=0.001		*P*=0.001		*P*=0.01
Calcification							
Present (10)	4 (40)	6 (60.0)	2 (20)	8 (80)	20 (20)	8 (80.0)	2 (20)
Absent (190)	97 (51.1)	93 (48.9)	20 (10.5)	170 (89.5)	4 (2.1)	186 (97.9)	2 (1.1)
	P=0.496		*P*=0.351		*P*=0.001		*P*=0.001
Infarction							
Present (05)	5 (100)	0	2 (40)	3 (60)	2 (40)	3 (60)	2 (40)
Absent (195)	96 (49.2)	99 (50.8)	20 (10.3)	175 (89.7)	4 (2.1)	191 (97.9)	2 (1.0)
	P=0.074		*P*=0.169		*P*=0.001		
Haematoma							
Present (32)	28 (87.5)	4 (12.5)	7 (21.9)	25 (78.1)	3 (9.4)	29 (90.6)	3 (9.4)
Absent (168)	73 (43.5)	95 (56.5)	15 (8.9)	153 (91)	3 (1.8)	165 (98.2)	1 (0.6)
	P=0.001		*P*=0.032		*P*=0.082		*P*=0.010

APS: Antiphospholipid syndrome, NICU: Neonatal intensive care unit

Table 4: Comparison of mean birth weight of babies in cases and controls in different studies

Study	Mild PE (kg)	Severe PE (kg)	Controls (kg)
Present study	2.49	2.24	2.64
Navbir *et al.* (2012)	2.79±0.42	2.59±0.28	3.27±0.46
Londhe and Mane (2011)	2.26		2.73
Majumdar *et al.* (2005)	2.04±0.48		2.8±0.32
Udainia and Jain (2001)	2.2		2.6

PE: Pre-eclampsia

controls. Findings are compared to other studies; we can observe it in Table 4. The mean F/P weight ratio was more in severe PE 6.15 ± 0.757 group than control group 5.89 ± 0.769. This correlates with Majumdar *et al.* which shows ratio of 5.89 ± 10.04 in control group and 6.23 ± 0.87 in hypertensive cases. Londhe and Mane study showed ratio of 7.23 ± 1.90 in hypertensive group compared to 6.79 ± 2.04 in controls. Zia-ur-rehman *et al.* study findings also show similar results. The same ratio was found less in the hypertensive group than

control group by Garg *et al.*, 1996 and Priya *et al.* 2012.[13] In present study cotyledon numbers were found to be significantly less in hypertensive group which is similar to the findings of the study by Sultana *et al.*, 2007.[14] Study by Majumdar *et al.* showed no significant difference between controls and cases.

In present study most common shape of the placenta observed was circular in severe PE the occurrence was 81 (91.0%) in mild PE it was 91 (91.0%). We also observed increased oval shaped placenta in PE group about 13% which was comparable with study of Kiswara *et al.* who found 40% oval placenta in PE group but most common shape found in study group was discoidal or circular. In a study by Navbir *et al.*[15] they found the shape of the placenta was discoidal in 73.33% of cases in the study group and 83.33% in the control group. Other shapes that were observed were irregular (16.67%) in study group and 10% in control group and bidiscoidal, lobed and diffused (3.33% each) in both study and control group. Shah *et al.* observed no clinical significance in oval or rounded shaped placenta. We observed increased incidence of marginal and eccentric cord insertion in PE group 15% compared to controls 5% this observation holds good with pretorius (1996) 55 who reported cases of marginal insertion of placenta in about 42% cases of pregnancy induced hypertension.

Calcification is regarded as evidence of placental senescence or degeneration. In present study incidence of calcification is increased in severe PE group 35% compared to mild PE 13% and controls 10%. Harsh *et al.* (1989) found frequency of calcification was same in control as well as in hypertensive group.[16] In our study, the overall incidence of calcification is more in severe PE compared to mild PE and controls. This is similar to study by Narasimha and Vasudeva (2011)[17] which showed the overall incidence was 26.9%, 22.2% in mild PE and slightly higher (33.3%) in severe PE. In the present study significant association found between calcification and NICU admission in control group. But we did not found any significance in study group this might be due to exclusion of still births findings from cross tabulation. This is similar to study conducted by Goswami *et al.* (2011)[18] which concluded that fetal outcome in terms of birth weight of newborn to mother having pregnancy induced hypertension and calcification of placentae (grossly and microscopically) was poor as compared to control group.

Infarction was seen in 48% of severe PE compared to 25% of mild PE and 5% of cases. This is in comparison with Masodkar *et al.*'s 40.4%[19] and Udainia *et al.* (2004) who had observed a similar increase in the incidence of placental infarction with severity of toxemia. In the case group the association of stillbirth and low birth weight with infarction was statistically significant, whereas no relation was noted in the low Apgar, NICU admission and presence of infarction. In control group there was statistically significant association between infarction and NICU admission. This is comparable with study by Salgado *et al.* where the difference in the birth weight of the newborns in hypertensive and normotensive groups in relation to placental infarction was statistically significant (2.2 vs. 3.1 kg, $P < 0.001$).

CONCLUSION

The hypertensive disorders of pregnancy adversely influence the morphology of the placenta. The pathological changes observed in placentae of patients with hypertensive disorders of pregnancy like RP hematoma and infarction adversely influence the perinatal outcome. However, none of these pathological changes of placenta are specific to hypertensive disorders of pregnancy but these pathological findings are significantly increased in cases of PE compared to controls.

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How to cite this article: Vijayalakshmi B, Kittali S. Morphological changes of placenta in cases of pre-eclampsia and perinatal outcome. Int J Sci Stud 2015;3(5):137-142.

Source of Support: Nil, **Conflict of Interest:** None declared.