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Original Research Article

Histological evaluation of placenta in hypertensive pregnancies

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ABSTRACT

Background: Maternal and fetal status are reflected in placenta. Toxemia of pregnancy exerts great impact on placenta and thereby fetal and maternal outcomes. Placenta reflects changes of toxemia and these changes are seen morphology as well as histology. Hence study of placenta gives information on the in-utero fetal condition.
Methods: A total of 1000 placenta, 500 each from hypertensive and normotensive groups were included in this study conducted in Anatomy Department of SBKS Medical College and Research Centre, Vadodara. Histological evaluation of the samples taken was done under microscope.
Results: Microscopic examination of the placenta revealed the presence of calcification, infarction, fibrinoid necrosis, villous hyalinization, syncytial knots and cytotrophoblastic cellular proliferation in both control and hypertension groups. In the present study, calcification was seen in 35.8% in the control group, while the same was seen in 53.8% patients in test group. Fibrinoid necrosis was seen in 48.8% patients in control group as against 69% patients in test group. Villous Hyalinization was seen in 7.40% and 21.4% patients in control and test groups respectively. On the other hand, syncytial knots were seen in 38% and 69% patients in control and test groups respectively. In test group, cytotrophoblastic cellular proliferation was seen in 69% patients while in control group, it was seen in 33.2% patients. Infarction was also seen in test (42.4%) and control (12.6%) groups.
Conclusions: Hypertensive disorders of pregnancy have significant effect on the histology of placenta and also influences the fetal outcomes.

Keywords: Histology, Hypertensive pregnancies, Microscopic examination, Placenta, Pre-eclampsia

INTRODUCTION

Placenta is a vital organ that connects the fetus and mother.[1] The survival and growth of fetus are dependent on the placenta that is normal formation, appropriate development and optimal functioning of the placenta.[2] Study of placenta reflects maternal and fetal status. Placenta of complicated pregnancies reflect changes that gives insight into the perils faced by fetus inside the uterus. As the pregnancy progresses the changes are reflected not only in morphology or morphometry of placenta but also in the histology.[3]

Around 5-10% of pregnancies are complicated by preeclampsia. Hypertension clubbed with proteinurea constitute pre-eclampsia. It is unique to pregnancy.[2] Origin of pre-eclampsia is unclear; however, humoral factors rather than neurogenic factors are thought to be its causative agents.[3] Pre-eclampsia causes significant morbidity and mortality in mother and fetus.

Under normal circumstances of implantation, trophoblastic cells invade walls of spiral arteries and destructs their muscular layer, converting them into sinusoid-like channels which carry large volume of blood to the intervillous space. These sinusoid-like channels are

resistant to vasomotor agents. This invasion of trophoblasts into walls of spiral arteries begin at around 16-20 gestational week and completes at around 24 weeks' time. This physiologic process is defunct in patients with preeclampsia.[2] Apoptosis of cytotrophoblast cells is the main cause; as due to the apoptosis of cytotrophoblast cells there is only superficial penetration of decidua preventing trophoblast induced remodeling in placental bed of around 30-50% spiral arterioles.[3,4] As a result of this, the spiral arteries offer resistance due to persistence of muscular and elastic tissues. The vessels remain responsive to vasomotor stimuli and fail to dilate.

Histologically it is seen that in preeclamptic patients, the mean luminal diameter of uterine spiral arterioles is less than one third to that seen in normal pregnancies. This causes decreased perfusion and ultimately infarction of placenta as gestation progresses thereby causing hypoxia and retarded growth of fetus.[5,6]

Thus, examining placenta provides understanding of fetal intrauterine experience.[6-9] With these aspects in mind, this study was conducted. Present study has been undertaken to assess the histology of placenta from mothers with pregnancy induced hypertension (PIH) and to correlate the findings with those from normal pregnancies.

METHODS

In the Anatomy Department of SBKS Medical Institute and Research Centre, Vadodara, this prospective, observational study was carried out, after obtaining ethics committee approval. The study was conducted for a period of five years i.e. January 2012 to December 2017.

Inclusion criteria

- Normotensive mothers and mothers with pregnancy induced hypertension (pre-eclampsia and eclampsia),
- Gestational hypertension.

Exclusion criteria

- All other maternal conditions which lead to small placental size,
- Placental infarcts and intra-uterine growth retardation.

Sample size

A total of 500 subjects with hypertensive pregnancies (test group) and 500 subjects with normotensive pregnancies (control group) were included.

Following delivery, Department of Obstetrics and Gynaecology that is part of Dhiraj Hospital, Piparia, Vadodara, a tertiary care hospital attached to S.B.K.S Medical Institute and Research Centre, informed the investigator about the delivery and brief history of the patient. Investigator/designee went to fetch placenta, other relevant information regarding subject was captured in screening proforma. Placentae were collected and brought to the Anatomy Department for the study. Placental collection continued till 500 placentae of normotensive mothers and 500 placentae of hypertensive mothers were collected.

Placentae with membranes were collected. Amnion and chorion were trimmed from the placenta. Umbilical cord was cut at a distance of about 40mm from the site of insertion. Following this, the placentae were washed and mopped.

The placental tissue was processed for preparing paraffin blocks and histological assessment. Microtome technique was used for sectioning tissue. Tissue samples were taken from the umbilical cord insertion site, from the margins at 12, 3, 6, 9'o clock positions and from center of the placenta, from umbilical cord, from the cut end and membranes and also from the site of fibrosis or infarction. After processing, tissue samples were stained with routine hematoxylin and eosin stain and fixed on glass slides. Sections were studied under microscope. Findings were recorded in the screening performa.

RESULTS

In the present study, 1000 placentae, 500 from normotensive and 500 from hypertensive mothers, were studied. In the hypertensive group, 25% subjects had gestational hypertension, 50% patients had pre-eclampsia and remaining 25% patients had eclampsia (Table 1).

In both the groups, there was predominance of primigravida with the same being 88.2% (n=441) in the normotensive group and 80% (n=400) in the hypertensive groups. 11.8% patients in normotensive groups and 20% patients in hypertensive groups were multigravida (Table 2).

Hypertensive group had significantly high blood pressure, the mean systolic blood pressure in the hypertensive group was 149.8±7.48mmHg, while mean diastolic blood pressure in the normotensive group was 91.14±4.14mmHg (Figure 1). In the hypertensive group, 65% subjects delivered at full term while 35% females delivered at pre-term, as against this in the normotensive group, 87.2% females delivered at full term while only 12.8% delivered preterm (Figure 2). Statistically, a significantly higher number ($p<0.05$) of females delivered pre-term in hypertensive group. However, a significant live birth were seen in both groups, but between the groups fetal mortality was high in hypertensive group (10%). Intrauterine growth retardation was predominant in hypertensive group with mean birth weight being 2.82±0.43kg in normotensive group and 2.33±0.84kg in hypertension group. NICU admission was significantly high in newborns of hypertensive mothers (58.6%) as against 2.8% in

normotensive groups (Table 3). Microscopic examination of the placenta revealed the presence of calcification, infarction, fibrinoid necrosis, villous hyalinization, syncytial knots and cytotrophoblastic cellular proliferation in both control and hypertension group.

Table 1: Distribution of cases.

Normotensive group	Hypertensive group									
	Gestational hypertension		Pre-eclampsia		Eclampsia		Total			
No.	%	No.	%	No.	%	No.	%	No.	%	
500	50	125	12.5	250	25	125	12.5	500	50	

Table 2: Gravida status of the patients enrolled.

Gravida status	Normotensive group		Hypertensive group	
	No.	%	No.	%
Primi gravida	441	88.2	400	80
Multi gravida	59	11.8	100	20
Total	500	100	500	100

Table 3: Fetal outcomes.

Parameters	Normotensive group	Hypertensive group
Live Birth	493 (98.6%)	450 (90%)
Intrauterine Deaths (IUD)	7 (1.4%)	50 (10%)
Birth weight (kg)	2.82±0.43	2.33±0.84
NICU admission required	14 (2.8%)	293 (58.6%)

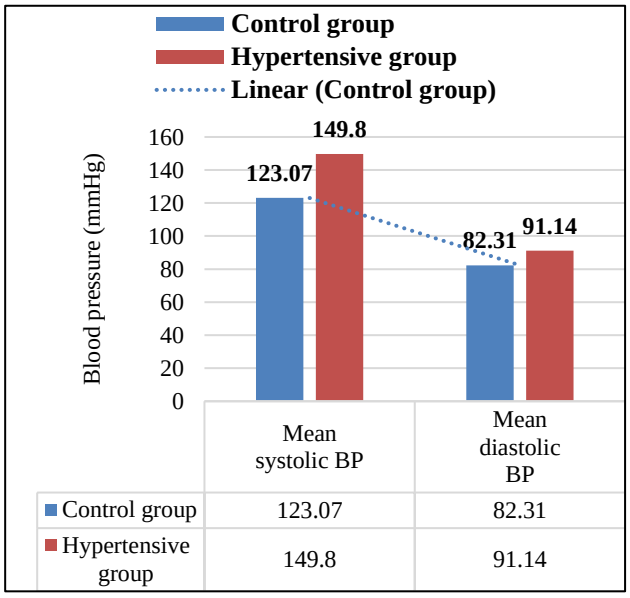

Figure 1: Mean blood pressure in control and hypertensive group.

Microscopic examination of the placenta revealed the presence of calcification, infarction, fibrinoid necrosis, villous hyalinization, syncytial knots and cytotrophoblastic cellular proliferation in both control and hypertension group.

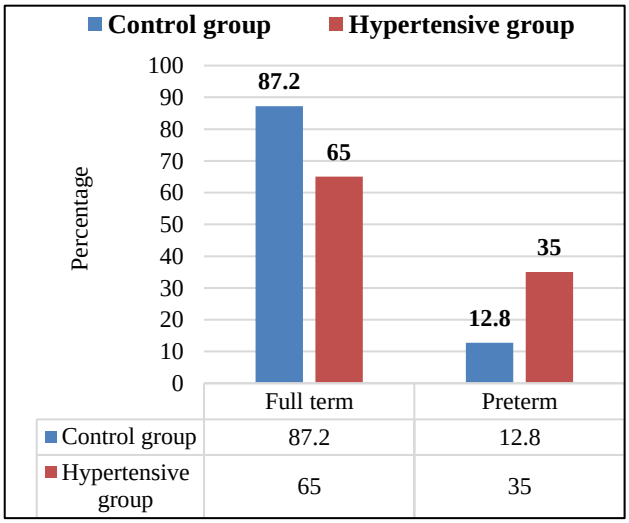

Figure 2: Term of delivery.

In the present study, calcification was seen in 35.8% in the control group, while the same was seen in 53.8% patients in test group. Fibrinoid necrosis was seen in 48.8% patients in control group as against 69% patients in test group.

Villous hyalinization was seen in 7.40% and 21.4% patients in control and test group respectively. On the other hand, syncytial knots were seen in 38% and 69% patients in control and test group respectively. In test group, cytotrophoblastic cellular proliferation was seen in 69% patients while in control group, it was seen in 33.2% patients. Infarction was also seen in test (42.4%) and

control (12.6%) group (Table 4). Thus, a significant impact of hypertension on placental histologylogy and its resultant impact on fetal growth as compared to normotensive patients was observed.

Table 4: Microscopic examination findings of placenta.

Parameters	Presence/Absence	Normotensive group		Hypertensive group		p-value
		N	%	N	%	
Calcification	Present	179	35.80%	269	53.80%	<0.05
	Absent	321	64.20%	231	46.20%	
Fibrinoid necrosis	Present	244	48.80%	345	69.00%	<0.05
	Absent	256	51.20%	155	31.00%	
Villous Hyalinization	Present	37	7.40%	107	21.40%	<0.05
	Absent	463	92.60%	393	78.60%	
Syncytial knots	Present	190	38.00%	345	69.00%	<0.05
	Absent	310	62.00%	155	31.00%	
Cytotrophoblastic cellular proliferation	Present	166	33.20%	345	69.00%	<0.05
	Absent	334	66.80%	155	31.00%	
Infarction	Present	63	12.60%	212	42.40%	<0.05
	Absent	437	87.40%	288	57.60%	

DISCUSSION

Hypertensive disorders of pregnancy exert profound impact on the histology of placenta and thereby have impact on fetal outcomes. In the present study, in both the groups, there was predominance of primigravida. Primigravida is one of the etiologic factors of PIH and this was confirmed in our study as majority of patients were primigravida. This finding is also confirmed by other investigators such as Siva Sree Ranga. MK, et al, Kambale T and Kheir AEM, et al.[10-12] Hypertensive group had significantly high blood pressure. Kumari P et al, has reported significantly high blood pressure in hypertensive group as compared to normotensive just as it was observed in our study.[13] Similar to present study, preterm deliveries were high in hypertensive groups in the published literature. Study by Adu-Bonsaffoh K et al, in Ghana showed that 21.7% pregnancies were delivered preterm while the mean duration of gestation was 37 weeks in the study by Pokorna V et al.[14,15]

A significant live birth was seen in both groups, but between the groups fetal mortality was high in hypertensive group (10%). Authors report a higher still birth in hypertensive pregnancies similar to study by Allen VM et al, wherein it was observed that women with any hypertension in pregnancy were 1.4 times more likely to have a stillbirth as compared with normotensive women.[16]

Authors observed low birth weight in babies of hypertensive mothers. This was in concurrence to the findings of Rahman LA et al, who reported that there was a significant association of pregnancy-induced hypertension with low birth weight and that women who delivered low birth weight babies were five times more likely to have had pregnancy-induced hypertension.[17] In the study by Keche HA et al. the mean birth weight was 2813.60±258.06 g in normotensive group, while it was 2141.00±439.69g in hypertensive group.[18]

Present study found that significant proportion of newborns of hypertensive mothers (58.6%) required Neonatal Intensive Care Unit (NICU) admission, this was similar to Adu-Bonsaffoh K et al, study conducted in Ghana wherein 24.7% neonates were admitted to the Neonatal Intensive Care Unit.[14] Habli et al, reported that the rate of neonatal intensive care unit admission (25.6% vs 8.7%) was greater in hypertensive pregnancies that delivered at 37 weeks of gestation.[19]

Microscopic examination of the placenta revealed the presence of calcification, infarction, fibrinoid necrosis, villous hyalinization, syncytial knots and cytotrophoblastic cellular proliferation in both control and hypertension group. In the present study, villous hyalinization was seen in 7.40% and 21.4% patients in control and test group respectively while fibrinoid necrosis was seen in 48.8% patients in control group as against 69% patients in test group. Fibrinoid necrosis that is seen in placental villi is a characteristic feature of pre-eclampsia. It appears, initially, in the trophoblast as a small “blob” of homogenous material that is external to the basement membrane and deep to the syncytiotrophoblast. This then enlarges, more towards basement membrane, without invading it, forming gradually deepening crescent in basement membrane, till the entire villus is replaced by fibrinoid material. Also, there is progressive degeneration of syncytium of the affected villus. Thus, a mass of structureless,

homogenous, acidophilic material is seen which is surrounded by few degenerate syncytial nuclei. It is believed that fibrinoid necrosis results from replacement of villus with fibrin which is formed from maternal or fetal blood.[20-22]

In test group, cytotrophoblastic cellular proliferation was seen in 69% patients while in control group, it was seen in 33.2% patients. Infarction was also seen in test (42.4%) and control (12.6%) group. Syncytial knots were seen in 38% and 69% patients in control and test group respectively. Fox, in 1965, observed that, syncytial knot formation is related to length of gestation and is an indicator of placental maturity, when it is within limits. He also observed that excess syncytial knot formation is associated with reduced foetal circulation through the villi, irrespective of the mechanism.[23]

Table 5: Microscopic examination of placenta of current study as compared to available literature.

Parameters	Current study		Siva Sree Ranga. MK et al[10]		Narasimha A et al[27]		Kambale T et al[11]	
	N (%)	H (%)	N (%)	H (%)	N (%)	H (%)	N (%)	H (%)
Calcification	35.8%	53.8%	23.3%	56.7%	8.10%	77.7%	-	-
Fibrinoid necrosis	48.8%	69%	0	63.3%	29.72%	37%	4.4%	38.4%
Villous Hyalinization	7.4%	21.4%	0	16.7%	10.8%	14.8%	-	-
Syncytial knots	38%	69%	23.3%	63.3%	45.9%	70.3%	20%	38.4%
Cytotrophoblastic cellular proliferation	33.2%	69%	10%	63.3%	-	62.96%	15.6%	38.4%
Infarction	12.6%	42.4%	6.7%	36.7%	10.8%	22.2%	-	-

N - Normotensive group; H- Hypertensive group.

Thus, reduced fetal blood flow through villi results in stromal fibrosis and excess syncytial knot formation. Degree of stromal fibrosis and syncytial knots correlates with degree of reduction in villous perfusion. Placental hypoxia seen in hypertensive pregnancies causes' parenchymal cells loss that appears as syncytial knots; this also causes synthesis of fibrous tissue in place of parenchymal cells. Fibroblasts present in stroma synthesize fibrous tissue which causes subtrophoblastic basement membrane thickness. Stasis of the maternal blood in the intervillous space causes subchorionic fibrin deposit. These findings were also confirmed in a study by Harianne et al, wherein statistically significant level of stromal fibrosis was seen in cases of toxaemia as well as anaemia (P <0.01), thus implicating placental hypoxia as a root cause of stromal fibrosis, basement membrane thickening and syncytial knot formation.[24]

Placental infarction of <5% is common, however, >5% is abnormal and is caused by occlusion of maternal uteroplacental vessels due to thrombosis that occurs in toxemia.[25]

Calcification was seen in 35.8% in the control group, while the same was seen in 53.8% patients in test group. Placental aging or degeneration is reflected from calcification that is seen.[26]

The findings of the current study are also confirmed by other similar studies (Table 5).[10,11,27]

Thus, a significant impact of hypertension on placental histology and its resultant impact on fetal growth as compared to normotensive patients was observed.

CONCLUSION

Hypertensive disorders of pregnancy exert profound impact on the histology of placenta and thereby have impact on fetal outcomes. Study of placenta helps evaluate the prenatal experience of the fetus and predict fetal outcome.

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