
Paper

Placental changes in pregnancy induced hypertension

R.P Pathiraja¹, S. K Senanayake², K Samarasingha²

Abstract

Objective: To study the histomorphological changes in placentae of pre-eclamptic mothers and to compare them with placentae of normotensive mothers.

Method: This study was carried out in 34 placentas of mothers who had pregnancy induced hypertension (PIH) and 34 placentas of normotensive non diabetic mothers in the Department of Pathology, University of Sri Jayewardenepura. Placentae were fixed in normal saline for 48 hours. After fixation the placentae were divided into four quadrants and 5mm pieces of tissue were taken from the center, upper and lower quadrants. After tissue processing and staining, the histomorphological changes were studied in both normotensive and hypertensive groups after obtaining clinical details from the bed head tickets.

Results: Infarctions, small villi and numbers of syncytial knots and vasculosyncytial membrane were significantly higher in the study group

compared with the control group. The severity of hypertension correlated with the extent of the placental infarcts.

Conclusion: A significant number of both macroinfarcts and microinfarcts with an increased number of syncytial knots was observed in the hypertensive group as compared to normotensive group which may be due to placental hypoxia.

Key Words: Placenta, Pre-eclampsia, Syncytial knots, Vasculosyncytial membrane.

Introduction

The placenta is the interface between the foetus and the mother. The survival and growth of the foetus is essentially dependent on the formation and the full development of the placenta. It undergoes changes in weight, volume, structure, shape and function continuously throughout gestation to support the prenatal life⁽¹⁾. The examination of the placenta in utero as well as postpartum, gives

Departments of¹Obstetrics & Gynaecology and²Pathology, Faculty of Medical Sciences, University of Sri Jayewardenepura, Gangodawila, Nugegoda

Correspondence: R. P. Pathiraja, Department of Obstetrics & Gynaecology, Faculty of Medical Sciences, University of Sri Jayewardenepura, Nugegoda. E. mail : ramya_pathiraja@yahoo.com

valuable information about the state of the foetal wellbeing and this information is useful in the management of complications in the mother and the newborn⁽²⁾. In cases of poor pregnancy outcome and certain maternal disorders, proper placental examination will provide useful information to the obstetrician and the neonatologist⁽³⁾.

Pre-eclampsia affects approximately 3% of all pregnancies worldwide⁽⁴⁾. Although much research into the aetiology and mechanism of pre-eclampsia has taken place, its exact pathogenesis remains uncertain. The main functional units of the placenta are the chorionic villi. Within them, the foetal blood is separated from the maternal blood in the surrounding intervillous space by vasculo-syncytial membranes overlying dilated foetal capillaries^(5,6). In the normal pregnancy, capillary growth is biphasic, with branching angiogenesis and formation of tightly looped capillaries, followed by a phase of increased non-branching angiogenesis with the formation of longer capillaries^(7,8).

In hypertension, the utero-placental circulation is compromised and the villi are exposed to a more focal hypoxia resulting in a shift towards branching angiogenesis^(9,10). Syncytial knots are aggregates of syncytial nuclei at the surface of terminal villi. These knots increase in number with increasing gestational age. It is also increased in conditions

of utero-placental malperfusion such as in preeclampsia⁽¹¹⁾.

Infarctions are commonly seen in placentae from pregnancies complicated by pre eclampsia and the extent and incidence of infarction increases with the increasing severity of toxemia. The exact relationship between the placental surface area, the extent of infarction and foetal distress is not clear⁽¹²⁾. Thus, this study was carried out to describe the histomorphological features in the placentae of pre-eclamptic mothers and to compare these with placentae of normotensive mothers.

Materials and Methods

The study was conducted at the Department of Pathology in collaboration with the Department of Obstetrics and Gynaecology, University of Sri Jayewardenepurara from February 2011 to August 2011. Placentae expelled during normal delivery and during caesarean section were included in the study.

The study group comprised 34 placentae from pregnant women of 30 to 40 completed weeks, who had a blood pressure at or above 140/90 mmHg on at least two occasions 6 hours apart after 20 weeks of gestation, with or without oedema and/or proteinuria. The results were compared with those of 34 placentae of singleton pregnancies of normotensive mothers who were not diabetic from the same unit, collected randomly and of a similar period of amenorrhoea (POA) of 30 to 40 weeks.

All placentae were collected after delivery. Immediately after the delivery of the foetus, two clamps were applied. One was applied near the vulva in case of a vaginal delivery and at the uterine incision in case of a caesarean section. In both instances the second clamp was applied six inches from the umbilicus to prevent transfer of blood to or from the placenta. Controls, which needed an injection of ergometrine before the delivery of the placenta, were excluded from this study as strong uterine contraction might alter the placental weight by forcing blood into it.

After delivery of the placenta a ligature was applied to the cord near its insertion into the placenta and both membranes and cord were cut within 1 cm of the placenta. This was then gently washed in running tap water to remove excess blood and liquor-amnii. Any abnormality of the cord and membranes was noted. The placenta was then wiped and weighed on an accurate commercial scale. The baby's weight was also recorded. The placentae along with the cords were fixed in 10 % formalin solution.

Histological examination

The foetal surface, maternal surface and cut surface of the placentas were examined and 3-6 full depth sections from the center, upper and lower quadrants. In addition, macroscopically abnormal pale white firm area and haemorrhages were measured and sampled. Sections were examined microscopically after staining with haematoxylin and eosin.

Presence of infarcts was confirmed by microscopic examination (Fig: 1) and its maximum dimensions were measured. Size of infarcts were divided into three categories depending upon the maximum dimension and accordingly less than 1cm infarcts were considered as mild and infarcts more than one cm in maximum dimension were considered as moderate. If more than 25 % of total surface area of placenta, it was infarcted considered as severe. These were further categorized into macroinfarcts and microinfarcts. Severe infarcts involving >25% of the surface area of the placentae were categorised as macroinfarcts while mild and moderate infarcts were categorised as microinfarcts.

Microscopic analysis of villous syncytial knots was done by counting the number of syncytial knots in 100 intermediate and terminal villi. Counting was done in areas where the highest amount of syncytial knots was easily visible on low power magnification. (x10). The distinction between a true syncytial knots and nuclear aggregates resembling knots (false knots) was subjective and ideally immunohistochemistry should be performed for confirmation. However, knots displaying highly condensed chromatin were considered as true knots (Fig: 2) According to the literature, PIH placentae show more than 30% syncytial knots compared to normal placentae.^(9,11)

The number of terminal villi per high power field was counted after identifying terminal villi by the criteria of thinned trophoblastic lining, lack of muscularised arterioles and more than 50% of the cross sectional area being occupied by vessels.⁽¹²⁾ The appropriate high power field was selected by considering the maximum amount of terminal villi to be included in to the field and the diameter of the villi measured approximately under high power. The diameter of a normal terminal villus is 40-100 micrometers.⁽⁷⁾ An increased number of villi in a high power field was taken as small villi. (Fig: 3) .

Vasculosyncytial membrane (VSM) being the primary site of fetomaternal exchange is formed when syncytiotrophoblasts surround the terminal villi in close contact with capillaries. In mature normal placenta, the villous syncytiotrophoblasts are thin measuring 1-0.5micrometer in thickness, devoid of nuclei and lie directly opposed to sinusoidally enlarged parts of the foetal capillaries. These membranes appear as thin blister like protrusions on the villous surface and form the only physical barrier between foetal and maternal blood ⁽¹²⁾. The presence or absence of thickened VSM was detected under high power examination of terminal villi. Those terminal villi having thick membranes with syncytiotrophoblastic nuclei were considered as thickened membranes.

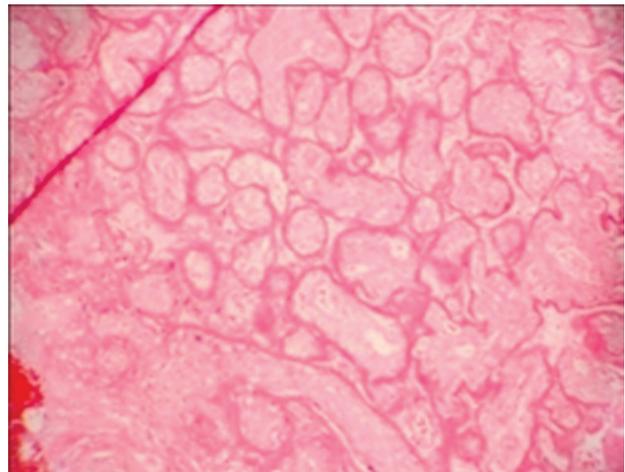


Fig. 1. Low power photomicrograph of a placental infarct. (H&E x 100)

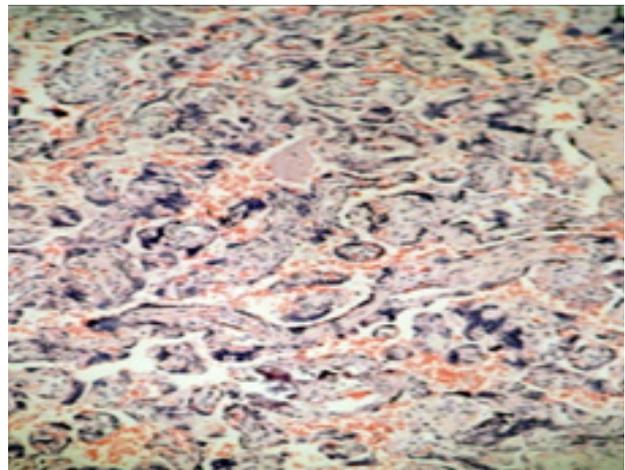


Fig. 2. Placental villi with syncytial knot formation (H & E x100)

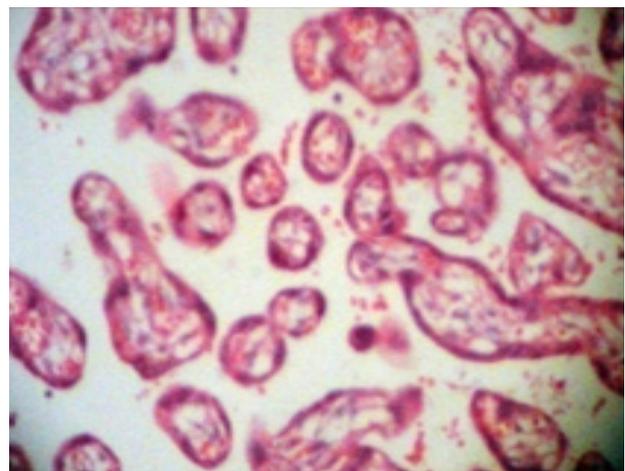


Fig.3 . Placenta of PIH mothers exhibiting small terminal villi (H & E x400)

Data analysis was done using SPSS (Version16) statistical package. In the comparison of results between PIH and normotensive mothers, a test was used for continuous data and a Chi-squared test was used for categorical data. A p value <0.05 was considered significant.

Results

The differences in maternal age, and the period of amenorrhoea (POA) between PIH and normotensive mothers are shown in Table 1. These results were not statistically significant. The differences in mean placental weight and mean birth weight of babies between the PIH

group and the comparison group are shown in the Table 2. These results were not statistically significant.

A significant amount of infarcts were seen in the placentae of mothers with PIH compared to normotensive mothers and the majority (65%) of these infarcts was mild to moderate in size and were categorized as microinfarcts. Small villi (82.4%) and syncytial knots (98.2%) were significantly increased in mothers with PIH. Vasculo-syncytial membranes were present in all mothers with PIH compared to the normotensive mothers and this was statistically significant.(Table 3)

Table 1 Comparison of age and POA of mothers between PIH and comparison groups

	PIH	Normal	Mean difference and	p
	Mean(SD)	Mean(SD)	95% CI	
Age(years)	31.15(4.94)	29.18(5.96)	1.971(-0.68, 4.62)	0.143
POA(weeks)	37.26(2.56)	37.68(2.41)	-.412 (-1.62, 0.79)	0.497

Table 2. Placental weight and birth weight of the babies between PIH group and comparison group

	PIH	Normal	Mean difference and	p
	Mean(SD)	Mean(SD)	95% CI	
Placental weight (g)	363.24 (128.40)	366.47 (111.24)	-3.24 (-61.41, 54.94)	0.91
Birth weight (g)	2653.17 (765.53)	2838.24 (398.11)	-185.07(-484.87, 114.73)	0.222

Table 3 Histological features in placentae of PIH and normotensive mothers

Histological Feature	PIH	Cases	Controls		Chi Square	df	p value
	No	%	No.	%			
Infarctions							
- Present	20	58.8	7	20.6	10.381	1	<0.001
- Absent	14	41.2	27	79.4			1
Size of the infarcts							
- Microinfarcts	13	65.0	5	71.4			<0.57
- Macroinfarcts	7	35.9	2	28.6			1*
Presence of small villi							
- Present	28	82.4	9	26.5	21.402	1	<0.001
- Absent	6	17.6	25	73.5			1
Increased syncytialknots							
- Present	30	88.2	18	52.9	10.200	1	<0.00
- Absent	4	11.8	16				47.1
Vasculo-syncytialmembrane							
- Present	34	100	29	85.3			<.027*
- Absent	0	.0	5	14.7			

* Fisher's exact test.

Discussion

Histopathological examination of the placentae of every birth is important as it may have implications for the child, future pregnancies and potential medico legal issues⁽¹⁾. Maternal and neonatal disorders has little

influence on the likelihood of the placenta being submitted for evaluation.⁽²⁾

The mechanism of poor utero-placental circulation associated with pre-eclampsia resulting in a small foetus remains obscure. All babies born to women with pre-eclampsia were

not small for dates⁽³⁾. In our study, even though the minimum weight of babies in mothers with PIH was low compared to the controls, this was not statistically significant. Interestingly, this has been noted even in the presence of lesions in the spiral arteries.⁽⁴⁾

There was no statistically significant difference of the mean weights of placentae between both groups in our study. This may be due to the compensatory hypertrophy of the placental mass following placental insufficiency secondary to inadequate utero-placental blood flow as described by Fox⁽⁵⁾ and Wigglesworth.⁽⁶⁾

Although the pathophysiology of pre-eclampsia remains undefined, placental ischemia is widely cited as a key factor.^(7,8) A significant number of both macroinfarcts and microinfarcts were seen in the placenta of hypertensive mothers in our study. Syncytial knots following oxidative stress associated with uteroplacental malperfusion were seen in a significant number of mothers with hypertension compared to normotensive mothers.^(9,10,11) The placenta can withstand infarction of more half of its substance without any deleterious effects on the foetus¹² and this may be the reason that our data did not reveal any significant differences in the birth weights of babies in the two groups.

A thickened vasculo syncytial membrane is found in normal placenta but a marked

thickening of trophoblastic basement membrane is associated with various pathological conditions such as pre-eclampsia^(13,14). In our study, there was a significant difference in the detection of vasculosyncytial membranes among the two groups.

Conclusion

Placental pathology was of little or no clinical value if there was no clinical indication for its examination⁽¹⁵⁾. However, placental pathology now plays an important role in obstetric litigation and its role in medico legal cases is well described^(16,17,18,19). There is insufficient data to support the placental examination of all live births⁽²⁰⁾. Placentae that were grossly abnormal or those which had clinical indications were recommended to be submitted for microscopic study. Hypertensive disorders in pregnancy influence the morphology of placentae which in turn adversely affect the perinatal outcome. This information can be useful in planning and management of future pregnancies.

If the mechanism of placental dysfunction in PIH and other intra uterine growth retardation (IUGR) associated complications is fully elucidated, it will certainly provide more precise disease-specific strategies.

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