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Study of Microscopic Features of Placenta In Pregnancy Induced Hypertension

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Abstract

Placenta plays an important role in fetal viability. Any abnormality in placenta reflects in fetal outcome. PIH (pregnancy induced hypertension) is one of the group which causes perinatal and maternal morbidity and mortality. Thus microscopic examination of placentae provides crucial information. Present study was carried out to study the microscopic features of placentae in normal pregnancies and in pregnancy induced hypertension which included total 100 patients (50 normotensive and 50 from PIH). All the placentae were examined microscopically. When results were analyzed it showed that there was statistical significance of syncytial knots, fibrinoid necrosis, cytotrophoblastic proliferation, calcification, hyalinization between two groups. Thus present study concluded that these microscopic abnormalities are seen in PIH patients which help to plan treatment accordingly to reduce fetomaternal bad outcome.

Keywords: Calcification, Cytotrophoblastic proliferation, Fibrinoid necrosis, Hyalinization, Syncytial knots.

Introduction

The Placenta is responsible for various functions like the respiratory, nutritional, excretory, endocrinal and immunological functions as transmission of antibodies. After delivery if the placenta is examined minutely it provides much insight into the prenatal health of foetus and the mother [1].

Placenta is an important factor in establishing the foetal damage resulting in bad pregnancy outcome irrespective of clinical care**.** Being an organ of vital importance for the continuation of a pregnancy and fetal nutrition, it has evoked great interest among anatomists, pathologists and the obstetricians. Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with haemorrhage and infection, that results in large number of maternal deaths and there off foetal deaths. Since all anabolites needed for foetal metabolism come from the mother's blood and foetal catabolites are passed back into the mother's circulation through the placenta. The examination of placenta gives a clear idea of what had happened with it, when it was in the mother's womb

and what is going to happen with the foetus in the future [2].

Hypertensive disorders during pregnancy are classified into 4 categories, as recommended by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy: 1) chronic hypertension, 2) preeclampsia-eclampsia, 3) preeclampsia superimposed on chronic hypertension, and 4) gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy. Pregnancy induced hypertension includes Gestational hypertension, Pre-eclampsia, and Eclampsia. In a multicentric study, approximately 30% of hypertensive disorders of pregnancy were due to chronic hypertension while 70% of the cases were diagnosed as gestational hypertension/preeclampsia. Thus the documentation of macroscopic and microscopic findings of placenta becomes essential [3].

Placental examination provides a diagnostic mean for various disorders that result for maternal and fetal morbidity and mortality like intrauterine growth retardation, neurodeveloepmental disorders etc [4,5]. Foetal distress, intrauterine foetal deaths and placental abnormalities are common in pregnancy induced hypertension (PIH). The risk is increased if placental function has been impaired by preeclampsia [6]. PIH causing more adverse outcome than any other systemic disorder. As the placenta is the mirror of maternal and foetal status, it reflects the changes due to maternal hypertension so placenta is the most accurate record of the infants prenatal experience. The histopathological examination of the placenta may provide crucial information regarding this. It is possible to highlight treatable maternal conditions and identify placental or fetal conditions that can be recurrent or inherited. Hence there is a need to observe the microscopic findings in placentae.

Aim and objectives

To study the microscopic features of placentae in normal pregnancies and in pregnancy induced hypertension.

Materials & Methods

The present study of placenta in pregnancy induced hypertension was done over the period of 2 years at department of Anatomy, Topiwala National Medical College, Mumbai,(MH) which included total 100 placentae, of which 50 were from normotensive cases and 50 were from pregnancy induced hypertension women of age group 20- 38 years and of any parity. Placentae in disease i.e chronic hypertension, pre-eclampsia or eclampsia superimposed on chronic hypertension and gestational diabetes were excluded from the study.

After due consent, the relevant clinical information of mother and babies were noted. All placentae were examined after fixation in 10% formalin overnight and sections were taken from representative areas, processed, stained with hematoxylin and eosin stain and studied for microscopic findings like syncytial knots, fibrinoid necrosis, cytotrophoblastic cellular proliferation, calcification, and hyalinization.

Results

Table no1: Showing statistics & comparison of all microscopic findings per low power field in group I (normotensive) & group II (PIH)

The data was analysed by SPSS 16.0 for windows evaluation version software. The independent t-test and Mann-Whitney U- test were used for statistical difference determination between the 2 groups.

Note: 1) p-value of 1.48E-07 is 1.48 X 10-07 or 0.000000148

2) IQR= Interquartile Range (i.e. 75th Percentile-25th Percentile**)**

^ All data failed 'Normality' test. Hence Mann-Whitney test was applied. T-value replaced by Z-value.

Table 1:

Variables ^	Groups	Mean	SD	Median	IQR	z - value	p-value
Syncytial knots (per low power field)	Group I	7.48	2.45	7.00	3.00	-8.502	1.86E-17
	Group II	18.70	4.28	18.00	6.00	Difference is significant	
Fibrinoid necrosis (per low power field)	Group I	1.80	2.10	1.00	3.00	-3.986	6.73E-05
	Group II	5.58	4.50	6.00	9.00	Difference is significant	
Cytotrophoblastic cellular proliferation (per low power field)	Group I	3.14	2.59	3.00	2.75	-7.718	1.19E-14
	Group II	9.22	2.59	9.00	4.00	Difference is significant	
Calcification (per low power field)	Group I	1.26	1.07	1.00	1.25	-6.322	2.58E-10
	Group II	4.40	3.58	3.00	2.25	Difference is significant	
Hyalinization (per low power field)	Group I	2.04	2.53	1.00	3.00	-8.389	4.90E-17
	Group II	12.72	4.09	12.50	6.00	Difference is significant	

In the present study, mean number of areas of syncytial knot formation in group I was found to be 7.48±2.45 while that in group II was 18.70±4.28 while Mean no of areas of fibrinoid necrosis per low per field in group I was found to be 1.80±2.10 while that of in group II was 5.58±4.50. This difference was statistically significant. This indicates that there was increased in no of areas of fibrinoid necrosis in PIH group.

In the present study, mean number of cytotrophoblastic proliferation per low power field in group I was 3.14±2.59 and in group II it was 9.22±2.5. This observation suggests that there is increase in cytotrophoblstic cellular proliferation in PIH cases.

Present study revealed that in placenta mean number of areas of calcification per low power field in group I was 1.26±1.07 while in group II it was 4.40±3.58. Thus there is increase in areas of calcification in PIH patients. In present study, mean number of areas of hyalinization per low power field in group I was 2.04±2.53 while in group II it was 12.72±4.09. The difference between two group was statistically significant. Thus it indicates that there was significant increase in areas of hyalinization in PIH group.

Discussion

Placenta has been often described as the mirror of the perinatal life as it depicts the most accurate record of the prenatal experience of an infant [7]. A glance at the literature reveals that the preeclampsia eclampsia syndrome exerts its deleterious effects on the placenta that can be observed microscopically. The present study was carried out to analyze and assess the significance of villous and stromal abnormalities by histopathological methods because these changes serve as a guide to the duration and severity of disease.

The histological examination of chorionic villi, showed an increase in number of syncytial knots, which is a feature of normal pregnancy. Syncytial knots (FIG: I) are focal clumps of syncytial nuclei that protrude into the intervillous space from the surface of villi. They are uncommon before 32nd week of gestation, after which

they increases rapidly in number until term. Formation of knots on more than third of the villi is considered excessive. There is an overall increase in syncytial knots formation with advancement of pregnancy. Excessive formation of syncytial knots is a feature of placentae from pregnancy induced hypertension and diabetes.

Different authors suggested different mechanisms of pathogenesis for the formation of syncytial knots. Syncytial knots have been variously considered as a degenerative phenomenon; a form of syncytial hyperplasia; a manifestation of trophoblastic amoeboid activity; a response to trophoblastic ischaemia; incidental by-product of the development of vasculo-syncytial membranes in the syncytiotrophoblast.

On light microscopy the nuclei in syncytial knots are seen to be small and densely staining. The ultrastructure findings suggest that the oldest nuclei in the syncytium are eventually aggregated together to form syncytial knots, which may be therefore considered to represent a sequestration of unwanted aged nuclei. It acts as an internal strut system which may help to protect the villous capillaries from the effects of sudden changes in the intervillous space pressure changes during labour. The presence of syncytial knots has been taken as an index of placental maturity. Excess of syncytial knots is due to reduced fetal perfusion and that in pregnancy induced hypertension the tendency towards an increased formation of knots is a consequence of the obliterative changes in foetal stem arteries which are the characteristic feature of such placentae. An excess of syncytial knots may be considered to be a response to placental ischaemia [8]. Similar findings were noted by various authors. Motwani R. et al found increase in syncytial knots per 100 villi in PIH group as 70.36 ± 13.34 and in normotensive group it was 26.93 ± 10.49. Kulandaivelu R. A. et al found increase in syncytial knots >30% in one field in PIH group than in normotensive group. Kartha S. et al considered more than 125-150 syncytial knots per 100 villi were considered as significant. 32% of PIH cases showed this finding whereas 16% of control group showed the same finding. In overall accelerated villous branching, numerous syncytial knots, and villitis are the related findings of reduced perfusion. According to Burton et al, generation of reactive oxygen species under oxidative stress could be the major reason of abnormal vascular remodeling and production of increased syncytial knots [9,10,11,12].

Fibrinoid necrosis (FIG 2) lesion is a very characteristic and easily recognizable. The first step in the evolution of this abnormality is the appearance of a small ‘blob’ of homogenous, acidophilic and strongly PAS positive material in the villous trophoblast at a site which is beneath the syncytiotrophoblast. This ‘blob’ of acidophilic material gradually enlarges and bulges progressively into the villous stroma. The blob does not actually invade the stromal tissue, for the underlying basement membrane remains intact although becoming increasingly indented into a crescentic shape, the concavity of which is progressively deepened by the expanding mass of fibrinoid material. This process continues until eventually the whole villus is converted into a fibrinoid nodule. So eventual appearance is that of a nodular mass of homogenous acidophilic material, around the periphery of which are a few degenerate syncytial nuclei. Any placenta in which more than 3 % of villi show fibrinoid necrosis is abnormal. Villous fibrinoid necrosis moderately increases in placentae from women with preeclampsia. Fibrinoid necrosis is assessed in villi, where villous stroma is replaced with

fibrinoid material and has been considered as a hallmark of an immunological reactions within the trophoblastic tissue [8]. Various authors found similar findings like Akhlaq M. et al found increase in mean no areas of fibrinoid necrosis in pre-eclampsia (84%), eclampsia (92%) cases and in normotensive cases it was 40%. [13]. Krielessi V.et al observed significant increase in fibrinoid necrosis areas in hypertensive group than normotensive group [14]. Motwani R. et al found increased fibrinoid necrosis per 100 villi in PIH group as 11.83 ± 4.3 and in normotensive it was 3.73±1.99. Kulandaivelu R. A. et al observed significant increase in fibrinoid necrosis > 5% in one field in PIH cases. Kartha S. et al found fibrinoid necrosis were obvious in the hypertensive group compared to the control group [9,10,11].

As pregnancy proceeds, both number and prominence of the villous cytotrophoblastic cells diminish and those remaining in mature villi are usually few in number, flattened, inconspicuous and irregular. They are commonly seen in about 20% of the villi. They never form a complete mantle around the villus as they do in immature placenta. There are two mechanisms for cytotrophoblastic cellular proliferation. It may be either by a failure of cytotrophoblastic regression or by proliferation of cytotrophoblastic cells. Sometimes failure of villous regression and some degree of cytotrophoblastic hyperplasia act together. The presence of numerous and proliferated cytotrophoblastic cells (FIG 3) is a feature of placentae from hypertensive disorders. In preeclampsia, the number of villous cytotrophoblastic cells increase progressively with the severity and duration of the disease. This proliferative activity in cytotrophoblast is a response to uteroplacental ischaemia. If placenta suffers an ischaemic damage as in PIH, cytotrophoblastic cells proliferate in an attempt to repair and replace the injured syncytial tissue [8]. This finding corroborates with findings Hina Nafees, Motwani R [8,15]. Motwani R et al observed mean no of areas of cytotrophoblastic cellular proliferation/lpf 3.46 ± 1.04 in normotensive group and in PIH group it was increased to 4.19 ± 1.15 [9].

Hyalinization (FIG 4) is a type of injury at the cellular level. It can be identified histologically as replacement of villous tissue by amorphous eosinophilic material. It may be either villous or stromal type. Motwani R. et al found mean number hyalinized areas in Group I was 13.33% and in Group II it was increased to 46.66% while Kartha S. et al noted increase in hyalinized areas in PIH group upto 28% than normotensive group having 16% [9,11].

Histological examination confirms the sites of calcium deposition, the mineral being readily recognized as structureless, basophilic material which is deposited either as plaque or as coarse granules which are strongly P.A.S positive and give positive reaction with Von kossa's stain. Calcification (FIG 5) may involve a single villus or may be widespread. The incidence of gross calcification varies from 14 to 37%. There are two forms of placental calcification the first 'physiological calcification' occurs during first 6 months of pregnancy in the form of tiny granules which are not visible to the naked eye, while the second 'dystrophic calcification' occurs during later months of gestation as plaque like deposits of easily visible calcium. Gross calcification is distinctly uncommon before 36th week of gestation, but then increases rapidly in incidence as term is approached. It may be a mark of placental senescence or degeneration [8]. Motwani R. et al observed areas of calcification in 36.66% in

normotensive group and in PIH group it was increased to 73.33% [9].

Conclusion

PIH is one of the cause that outrages the maternal and fetal mortality. Placenta being a foetal organ shares some stress and strain to which the foetus is exposed. Thus any disease affecting mother and foetus also has an impact on placenta. Present study showed that syncytial knots, cytotrophoblastic cellular proliferation, fibrinoid necrosis, calcified areas and hyalinization areas are significantly increased in pregnancy induced hypertension cases. Thus study of changes occurring in placenta in pregnancy induced hypertension may help us to understand better pathophysiological mechanism and design treatment plans for better maternal and foetal outcome

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Legends Figure

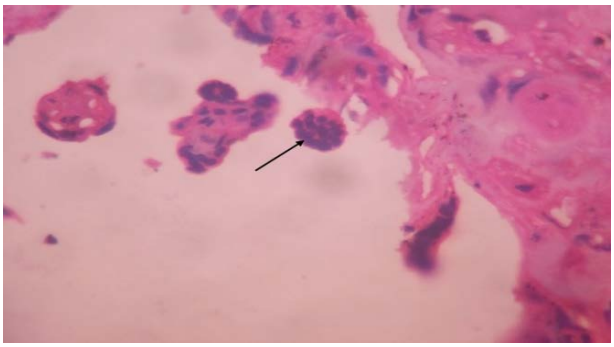

Fig. 1 :Syncytial knots H&E 40X

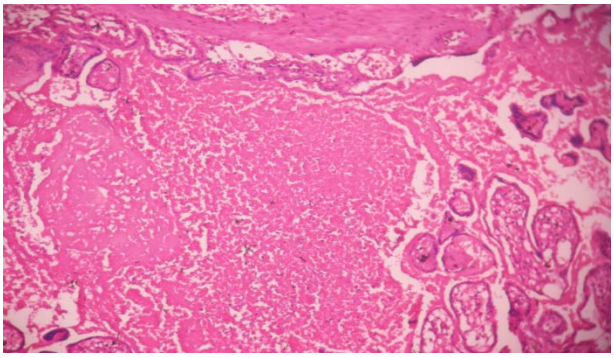

Fig 2: Fibrinoid necrosis H&E 40X

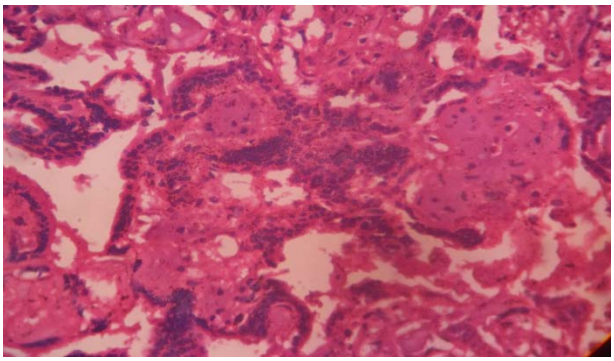

Fig 3: cytotrophoblastic proliferation H&E 40X

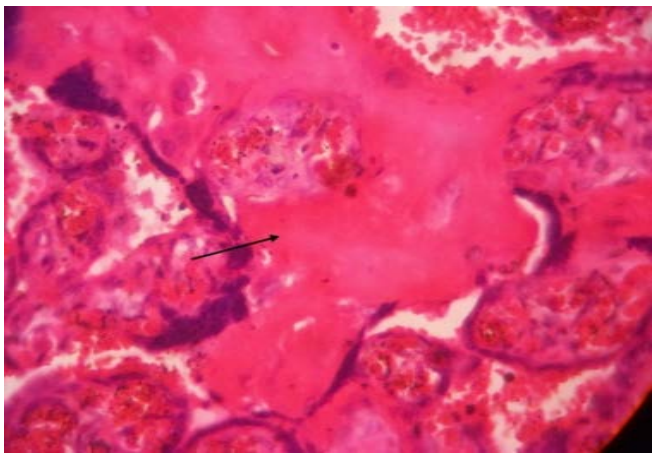

Fig 4: Hyalinization H&E 40X

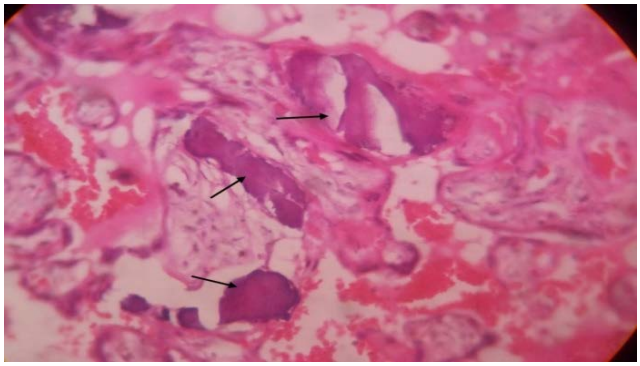

Fig 5: Calcification H&E 40X