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Original Research Article

Comparative study between histological changes in placenta from pre-eclampsia cases and normal pregnancy with special reference to cytotrophoblastic cell hyperplasia, villous stromal fibrosis and fibrinoid necrosis

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ABSTRACT

Background: Placenta is a vital organ and the most accurate record of the infant's prenatal experience. Pregnancy complications like hypertension significantly affect the placenta. Thus there is a need for thorough examination of it. Therefore the present study is dedicated to see the histological changes in placenta of pre-eclampsia with special reference to cytotrophoblastic cell hyperplasia, villous stromal fibrosis and fibrinoid necrosis and compared it with that of normal placenta.
Methods: Total 60 placentas were collected (30 from pre-eclampsia and 30 from normal pregnancy). Results were expressed in percentage after counting 100 villi. Data analysis has been done using Graphpad InStat 3 version and data is significant when p – value is <0.05.
Results: Mean no. of cytotrophoblastic cell hyperplasia, villous stromal fibrosis and fibrinoid necrosis in normal placenta are 10.1±5.01, 2.26±1.56 and 2.84±1.4 respectively and those in pre-eclampsia placenta are 36.82±16.15, 28.16± 34.42 and 8.22±1.44 respectively which are highly significant (p-value <0.001).
Conclusions: There is significant increase in number of cytotrophoblastic cell hyperplasia, villous stromal fibrosis and areas fibrinoid necrosis in placenta from pre-eclampsia cases than that of normal placenta. These changes may be due to vascular insufficiency which is usually occurring in pre-eclampsia.

Keywords: Cytotrophoblastic cell hyperplasia, Fibrinoid necrosis, Pre-eclampsia, Villous stromal fibrosis

INTRODUCTION

The placenta is a distinctive organ of higher mammals which is often disposed soon after parturition without adequate examination. It is the most accurate record of the infant's prenatal experience and appears like a mirror that reflects the intrauterine status of the fetus and postnatal foetal outcome.

Hypertensive disorders in pregnancy forms one part of the deadly triad along with haemorrhage and infection that contribute greatly to maternal and foetal morbidity and mortality. Foetus is dependent on the placenta for maintaining and promoting their normal development. Pregnancy complications like hypertension affect the placenta in a significant way both macroscopically and microscopically.

Several studies have shown that utero-placental blood flow is decreased in hypertensive disorders of pregnancy due to maternal vasospasm.[1] This leads to constriction of foetal stem arteries and has been associated with the changes seen in the placenta of these women.[2] Maternal vasospasm leads to foetal hypoxia and accordingly it may

lead to foetal distress and foetal death.[3] Recently, morphological changes in the chorionic villi have proven a relationship between placental pathology and foetal well-being.[4] It has been revealed that there is a clear relationship between confined placental mosaicism and foetal growth retardation.[5]

Thus there is a need for thorough examination of placenta to observe the effects of pre-eclampsia on the morphology of placenta. Therefore, the present study is dedicated to study the histopathological changes in placenta in preeclampsia with special reference to cytotrophoblastic cell hyperplasia, villous stromal fibrosis and fibrinoid necrosis.

METHODS

A total 60 placentae were taken, out of which 30 were from pre-eclamptic mother and other 30 from normal uncomplicated pregnant women. The study was done during the period of one year from September 2014 to August 2015.

Criteria for diagnosis of pre-eclampsia[6]

- Blood pressure of 140 mm Hg systolic or higher or 90 mm Hg diastolic or higher that occurs after 20 weeks of gestation in a woman with previously normal blood pressure.
- Proteinuria, defined as urinary excretion of 0.3 gm protein or higher in a 24 hr urine specimen or ≥1+ by dipstick method.

Exclusion criteria

- Placenta received from patients with condition other than pre-eclampsia.
- Placenta of patients with trophoblastic disease.

After delivery, each placenta was collected in a jar containing 10% neutral buffered formalin. After receiving the placenta, it was gently expressed so as to remove its blood content and then washed thoroughly under tap water, mopped with cotton pad. Then it was put again in 10% neutral buffered formalin for 48hours. After that, the parenchyma was sectioned in a "bread-loaf" fashion at approximately 1 to 2 cm intervals and examined for infarction, thrombi or excessive fibrin deposition. After that various sections were taken from the pathological part and stained with H & E stain. After that tissue section were examined under low and high magnification of microscope. Results were expressed in percentage after counting 100 villi. Data analysis has been done using Graphpad InStat3 version.

RESULTS

The present study included total 60 placentae, out of which 30 placentas were from normal term pregnancy and 30 from pre-eclampsia cases. The microscopic findings observed in placenta from pre-eclampsia cases and were compared with that of normal placenta with special reference to cytotrophoblastic cell proliferation, villous stromal fibrosis and fibrinoid necrosis.

Table 1: Comparison of cytotrophoblastic cell proliferation in placenta from normal and pre-eclampsia cases.

Microscopic findings	Normal placenta (Total = 30)	Placenta from pre-eclampsia (Total = 30)
Number of Cytotrophoblastic cell proliferation / 100 villi		
Less than 20%	27 (90%)	6 (20%)
20 – 40%	3 (10%)	8 (26.66%)
More than 40%	0	16 (53.33%)
Mean no. of cytotrophoblastic cell proliferation ± S.D	10.1±5.01	36.82±16.15
P- value	<0.001*	

* indicates that data is highly significant.

Cytotrophoblastic cell proliferation

Present study showed that cytotrophoblastic cell proliferation per 100 villi was less than 20% in 27(90%) cases of normal pregnancies and none of the any normal placentas showed cytotrophoblastic cell proliferation more than 40%. On the other hand 16 placentas i.e. 53.33% of pre-eclampsia cases showed cytotrophoblastic cell proliferation in more than 40% of villi (Table 1). Cytotrophoblastic cell proliferation is microscopically demonstrated in (Figure 1).

Villous stromal fibrosis

In the present study it was observed that only four placenta from normal pregnancies out of 30 cases showed villous stromal fibrosis which is less than 10% of villi.

While, out of 30 pre-eclamptic cases 16 i.e. 53.33% of cases showed villous stromal fibrosis (Table 2). Villous stromal fibrosis is microscopically demonstrated in (Figure 2).

Table 2: Comparison of villous stromal fibrosis in placenta from normal pregnancies and from pre-eclampsia cases.

Number of villous stromal fibrosis / 100 villi		
	Normal placenta (Total = 30)	Placenta from pre-eclampsia (Total = 30)
Absent	26 (86.66%)	14 (46.66%)
1 – 10%	4 (13.33%)	12 (40%)
More than 10%	0	4 (13.33%)
Mean no. of stromal fibrosis ± S.D	2.26±1.56	28.16±34.42
P - value	<0.001*	

* indicates that data is highly significant.

Table 3: Number of areas of fibrinoid necrosis in placenta from normal pregnancies and from pre-eclampsia cases.

Number of areas of fibrinoid necrosis / 100 villi		
	Normal placenta (Total = 30)	Placenta from pre-eclampsia (Total = 30)
Less than 3%	28(93.33%)	11 (36.66%)
3 -10%	2 (6.66%)	16 (53.33%)
More than 10%	0	3 (10%)
Mean no. of fibrinoid necrosis ± S.D	2.84±1.4	8.22±1.44
P- value	< 0.001*	

* indicates that data is highly significant.

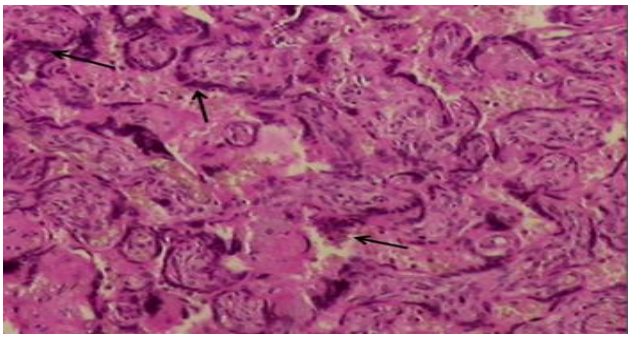

Figure 1: H & E section showing cytotrophoblastic cell proliferation (black arrow) in low power field (10x10x).

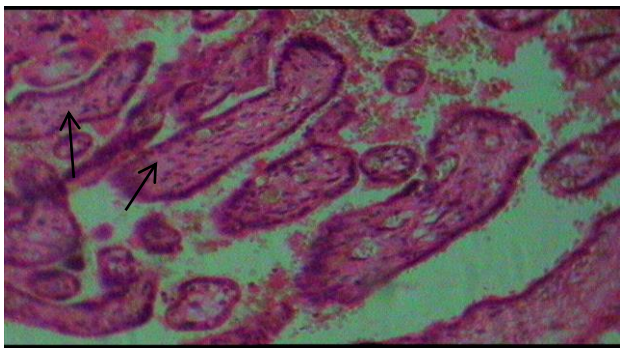

Figure 2: H & E section showing villous stromal fibrosis (white arrow) in low power field (10x10x).

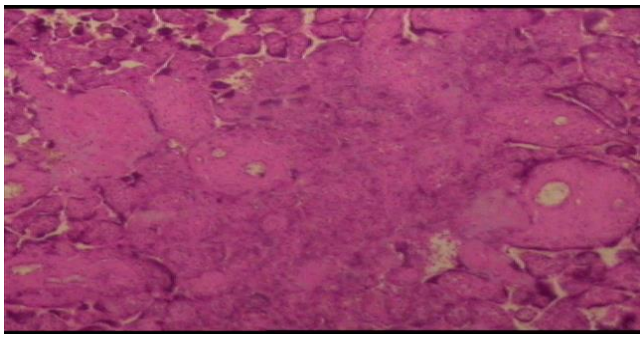

Figure 3: H & E section showing area of necrosis in low power field (10x10x).

Fibrinoid necrosis

In the present study it was observed that mean no. of fibrinoid necrosis in placenta from pre-eclamptic cases was 8.22±1.44 as compared to placenta from normal pregnancy it was 2.84±1.4 which is statistically significant (Table 3). Fibrinoid necrosis is micro-scopically demonstrated in (Figure 6).

DISCUSSION

The present study revealed that microscopic features like cytotrophoblastic cell proliferation, villous stromal fibrosis and fibrinoid necrosis are significantly increased in placenta from pre-eclampsia cases as compared to

placenta from normal term pregnancy. These findings corroborate well with that of the other studies.[7-9]

Fox reported that the cytotrophoblastic hyperplasia was seen strikingly in placenta of women suffering from pre-eclampsia eclampsia syndrome and it's presence could be correlated with high incidence of foetal hypoxia and intra-uterine death.[12] He suggest that if the syncytiotrophoblast suffers ischaemic damage, the cytotrophoblast will proliferate in an attempt to replace the damage tissue. Thus the degree of cytotrophoblastic hyperplasia is related to the severity of ischaemia. Genset in 1992 reported that cytotrophoblastic hyperplasia and excessive syncytial knot formation are seen in hypertensive disorders of pregnancy as invariable results of overall reduction of perfusion of the placenta.[13]

The changes were directly proportional to the severity of disease and perinatal outcome was worse with advancing grades of PIH. Fox in 1968 in their study "Fibrosis of placental villi" concluded that reduced foetal blood flow through the villi results in stromal fibrosis in toxaemic cases.[14] But Mathew et al found stromal fibrosis in 3% of villi in term placentae, claiming that this lesion may be a part of aging process.[15]

Fox reported that placentae from mature pregnancy should not contain villi with fibrinoid necrosis in more than 3% of villi. Relatively higher incidence of this lesion is reported in pregnancies complicated by hypertension.[16]

It is thought that this lesion is due to replacement of the villous by fibrin, this being formed either from the maternal blood in the intervillous space or from the foetal blood in the villous capillaries (Mckay et al, 1958; Wiggles worth, 1964).[17,18] Aetiological basis of this lesion appeared to be immunological reaction in the villous tissue. Hulka & Brinton claimed that high levels of antitrophoblastic antibodies may be found in the serum of pregnant women suffering from toxaemia.[19]

In 1978, Fox described histological abnormalities of the placental villi in pre-eclampsia after ultrastructural study. He pointed out that the characteristic response of the villi to a reduced maternal blood flow is proliferation of villous cytotrophoblastic cells and accompanying thickening of the trophoblastic basement membrane.

He suggested that this basement membrane protein is secreted by cytotrophoblastic cells and excessive proliferation of these cells leads to excessive production of basement membrane material.[20]

CONCLUSION

The present study revealed striking villous lesions like cytotrophoblastic cell proliferation, villous stromal fibrosis and fibrinoid necrosis in placenta from pre-eclampsia cases as compared to placenta from normal term pregnancy. These changes can be attributed to the reduced utero-placental blood flow which leads to foetal hypoxia, foetal distress and death which is usually occurs in hypertensive disorders of pregnancy.

From the present study it appears that pregnancy induced hypertension like pre-eclampsia adversely influence the morphology of the placenta and the comprehensive and quantitative estimation of placental changes are essential to understand the mechanism of placental dysfunction in detail. If this mechanism is fully elucidated, more precise intervention strategies can be devised and can contribute to more effective therapies in the future.

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