

Histopathological Study of Placenta in Pregnancy With Hypertension in western odisha.

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Abstract : The aim of my study is to compare the histopathological changes of placenta in preeclampsia with that of normal placenta and to analyze placental changes in the pregnancy induced hypertension. These changes serve as a guide to the duration and severity of disease. The material consisted of fifty term placenta collected from the labour room and operation theatre of the department of obstetrics and gynaecology, V.S.S. Medical College Hospital, Burla, after the normal or induced delivery of women clinically diagnosed as pre-eclampsia, severe pre-eclampsia, eclampsia, pre-eclampsia superimposed on essential hypertension and normal uncomplicated pregnancies as control. Different microscopic variants were observed on histological examination of the specimens. The striking villous lesion seen in toxemia of pregnancy were cytotrophoblastic cell proliferation. It was found that 65% of study group showed VSM deficiency. 72.5% cases of toxemia of pregnancy showed significant villous stromal fibrosis. Increased syncytial knot formation was seen in 82.5% of placentae of toxemia of pregnancy 77.5% of cases of toxemia of pregnancy showed fibrinoid necrosis. This study will help in understanding of the specific aetiologies of adverse outcome which will lead to specific treatment and preventive measures for those with risk for recurrence in subsequent pregnancies, specifically in pre-eclampsia and eclampsia cases.

Keywords: hypertension, placenta, pregnancy, stromal fibrosis

I. Introduction

Pregnancy Induced Hypertension (P.I.H.) is a matter of serious concern at present as regards to fetal outcome in pregnancy, as well as maternal morbidity and mortality. The exact etiology of hypertension in pregnancy is little known to medical fraternity. Toxemia of pregnancy, a multi system disorder, peculiar to pregnancy is characterised by gestational hypertension, proteinuria and activation of coagulation cascade with associated abnormalities in renal and hepatic function. Structural and functional derangement of placenta, evoke a considerable interest, as these may be the only yardsticks to measure adequacy of the foetal environment.

The foetus, placenta and mother consist the vital triad in pregnancy. Placenta is the most accurate record of the infants' prenatal experience¹.

Placenta in Latin means cake, that is floppy mass. Placenta is a vital organ for fetal development, derived from both foetal and maternal tissues, the maternal portion being the decidua basalis and the fetal portion is chorion frondosum.² It is basically meant for exchange of nutrients between maternal and foetal circulation to ensure an optimal environment for foetal growth and development^{3,4}. Common pathologies of pregnancy like intrauterine growth retardation, preeclampsia (pregnancy induced hypertension), are associated with incomplete vascular remodeling in the placenta⁵. Hypertensive disorders complicating pregnancy are common and form one of the deadly triads along with haemorrhage and infection, which result in large number of maternal deaths and thereof foetal deaths.

The present study intends to compare the histological changes of placenta in preeclampsia with that of normal placenta and to analyze placental changes in the preeclampsia-eclampsia syndrome. The histological examination will include a careful evaluation of the trophoblast, decidua and blood vessels. Pathological abnormalities that will be included are alteration of blood vessels (i.e. muscular hypertrophy of the media and fibrinoid changes in the vessel wall), inflammatory reactions (i.e. chorioamnionitis, villitis, villitis of unknown aetiology and funisitis), increased number of syncytial knots (>30%); changes in villous histology (i.e. thrombocytosis, fibrosis and haemorrhage); infarctions (at least two infarcts of ≥ 2 cm in diameter) and intervillous fibrin deposition.

As the placenta is the direct link between mother and foetus, the examination of placenta gives the 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. With this objective, the present study was carried out.

The present study was undertaken to analyze the quantitative placental changes in toxemia of pregnancy which included mild pre-eclampsia, severe pre-eclampsia and pre-eclampsia superimposed on essential hypertension. To compare and to correlate with the severity of maternal disease, the study of placenta from uncomplicated pregnancies were taken as control.

II. Materials and methods

The present study has been carried out in the department of Anatomy, V.S.S Medical College, Burla, Odisha, during the period from October 2011 to September 2013. The material consisted of fifty term placentae collected from the labour room and operation theatre of the department of obstetrics and gynaecology, V.S.S. Medical College Hospital, Burla, after the normal or induced delivery of women clinically diagnosed as pre-eclampsia (12cases),severe pre-eclampsia (10cases),eclampsia(14cases), pre-eclampsia superimposed on essential hypertension(4 cases) and normal uncomplicated pregnancies(10 cases) as control. Soon after the delivery, placenta was collected in a clean tray and umbilical cord, membranes and placental disc were examined sequentially.

2.1Preparation for histopathological Study

After thorough gross examination the placenta along with cord and membranes was kept in 10% formalin for a minimum period of 5 days, then sections were chosen for microscopic study in following manner.

1. Two sections of umbilical cord, one from foetal and the other from placental end were selected.
2. A thin strip of membranes, 2-3cm wide beginning from the point of rupture and extending to the nearest placental edge was chosen. A roll was made out of it with amniotic surface inside and a section from the roll was given for histopathological study.
3. Placental disc was placed on a flat surface with maternal side up. Before giving sections for microscopic study, placental parenchyma was again examined grossly by slicing perpendicular sections at 1 cm interval leaving the chronic plate intact. Presence of focal lesions like infarct, intervillous thrombi, excessive fibrin were noted. Minimum 4 sections of villus parenchyma which include two full thickness sections from midzonal area, two sections from central area and additional sections from grossly abnormal areas were submitted for histopathologic examination.

After selection of tissues, they were processed in automatic tissue processor and paraffin blocks were prepared. Sections of 5 micrometer thickness were cut. Numbers of slides were prepared for routine Haematoxylin and Eosin stain.

2.2Microscopic study

- A. Cord is examined for the presence of vessels its patency, any changes in vessel wall or oedema.
- B. Membranes are examined for any inflammation / abscess
- C. From placental disc random microscopic fields were selected from all slides and 100 villi were counted from each slide. The microscopic changes were expressed in percentage taken from the average of all sections and compared with that of uncomplicated pregnancies as controls. The different microscopic variants observed were Cytotrophoblast proliferation ,Villi showing Vasculo-Syncytial membrane,Trophoblastic basement membrane thickness Syncytial knotting ,Fibrinoid necrosis ,Stromal fibrosis ,Vascularity of villi.
- D. Confirmation of fresh and old infarcts.
- Calcification

III. Observation

Out of fifty singleton placentae undertaken for gross and microscopic analysis in the present series, 40 were in study group and 10 were in control group. The study group was further sub classified into grade I (Mild pre-eclampsia), grade II (Severe Pre-eclampsia), grade III (eclampsia) and grade IV (Pre-eclampsia superimposed on essential hypertension). The total number of cases in each grade has been shown in Table No. 1

Table – 1 Distribution Of Cases

Study group	Toxemia of Pregnancy	No. of cases (n)	Percentage of toxemia cases
Gr. I	Mild Pre-eclampsia (Mild PET)	12	30%
Gr. II	Severe Pre-eclampsia (Severe PET)	10	25%
Gr. III	Eclampsia	14	35%
Gr. IV	Pre-eclampsia superimposed on essential hypertension	4	10%
	Total no. of study group	40	100%
Control group	Uncomplicated pregnancies	10	100%

The control group consisted of ten placenta collected from women having no bad obstetrics history, no history of bleeding during pregnancy, duration of amenorrhoea corresponded to height of uterus and had normal foetal presentation. All of these were normotensive and their haematocrit values were within normal limits.

Microscopic Placental Alteration

The percentage of placentae showing abnormal villous count in different grades of toxemia of pregnancy has been shown in table II.

1. Cytotrophoblastic cell proliferation

All the cases of control group fell within the normal range of villi containing cytotrophoblastic cells (<20 percent) while 80 percent cases of study group had high villous count of these cells.

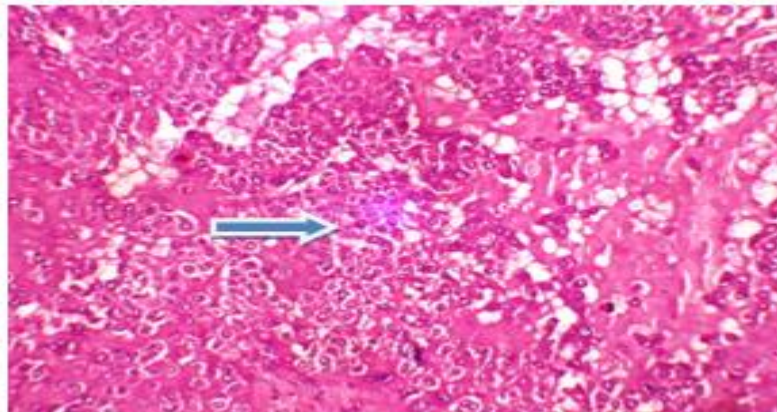


Fig 1.Microphotograph showing cytotrophoblastic proliferation H&E X100

2. Vasculo Syncytial Membrane (VSM) deficiency

65% of study group showed VSM deficiency (≤ 5 percent) while none of the controls showed this abnormality. The paucity of Vasculo syncytial membrane was seen in higher grades of toxemia correlating with the severity of the disease.

3. Villous Basement Membranes Thickening

None of the placentae from the control group showed undue basement membrane thickening (in excess of 3 percent villi) while 70 percent cases of study group revealed significant thickening. A direct correlation between the severity of the disease and this abnormality was observed.

4. Syncytial Knot Counts

More than 30 percent villi with syncytial knots were seen in placenta from 20 percent of control group while 82.5 percent cases of toxemia of pregnancy showed excessive syncytial knots formation. Maximum cases of enhanced syncytial knots were seen in cases of eclampsia and pre-eclampsia superimposed on essential hypertension.

5. Villous Stromal Fibrosis

Twenty percent placentae in control and 72.5 percent cases of toxemia of pregnancy showed significant villous stromal fibrosis.

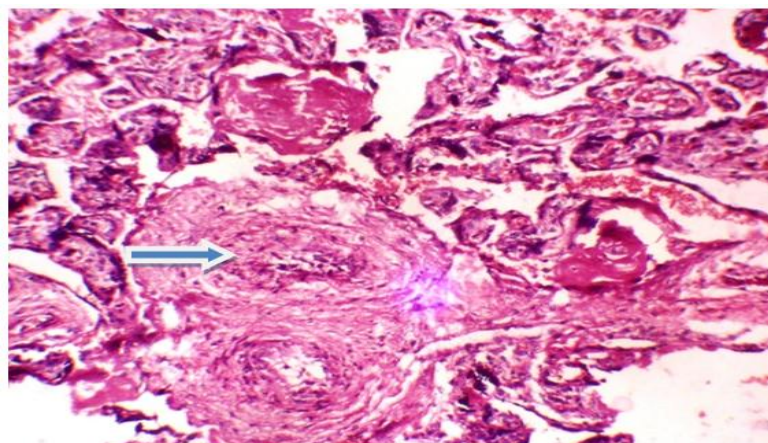


Fig 2 Microphotograph of placental villi showing stromal fibrosis with fibrinoid necrosis. H&E X100.

6. Villus Fibrinoid Necrosis

Significant villous fibrinoid necrosis was noted in 77.5 percent cases of toxemia of pregnancy and 20 percent cases of uncomplicated gestation.

7. Villous Vasculature

Placentae from majority of cases of control group (80 percent) as well as the study group (65 percent) were normally vascularised. However hypo and hyper vascularity too were seen in toxemia of pregnancy cases and control cases. Besides those above predominant villous changes observed in toxemia of pregnancy, few associated infrequent changes observed in some cases of toxemia were, obliterative endarteritis of foetal stem villous vessel seen in five cases of eclampsia and one case of pre-eclampsia superimposed on essential hypertension. From statistical analysis a significance of the microscopic lesions (Table II), it was observed that significant villous changes were seen in higher grades of toxemia of pregnancy i.e. severe pre-eclampsia, eclampsia and pre-eclampsia superimposed on essential hypertension

Table II Microscopic Villous Variant

Groups	Cyto proliferation		VSM		TBM Thickening		Syncytial Knotting		Stromal Fibrosis		Fibrinoid Necrosis		Villous Vasculature		
	≤20%	≥20%	≤5%	>5%	≤3%	>3%	≤30%	>30%	≤3%	≥3%	≤3%	>3%	Nor.	Hypo	Hyper
I(12) Mild PET	6	6	4	8	7	5	5	7	8	4	6	6	8	-	4
II(10)Severe PET	2	8	8	2	3	7	2	8	2	8	2	8	6	1	3
III(14) ECLAMPSI A	-	14	10	4	2	12	-	14	1	13	1	13	10	-	4
IV(4)Super- imposed on essential Hypertension	-	4	4	-	-	4	-	4	-	4	-	4	2	-	2
Total(40)	8	32	26	14	12	28	7	33	11	29	9	31	26	1	13
	20%	80%	65%	35%	30%	70%	17.5%	82.5%	27.5%	72.5%	22.5%	77.5%	65%	2.5%	32.5%
Control (10)	10	-	-	10	2	-	8	2	8	2	8	2	8	-	2
	100%			100%	20%	0%	80%	20%	80%	20%	80%	20%	80%		20%

IV. Discussion

The placenta has been described as the mirror of the perinatal mortality. A glance at the literature reveals that the preeclampsia-eclampsia syndrome exerts its deleterious effects on the placenta. So, the present study was undertaken to analyse placental changes in the Pre eclampsia eclampsia syndrome with a view to assess the significance of villous abnormalities by histopathological methods because these changes serve as a guide to the duration and severity of disease. The majority of cases of various grades of toxemia of pregnancy were found in younger age range and in primigravida. The striking villous lesion seen in toxemia of pregnancy were cytotrophoblastic cell proliferation. Most of the cases of eclampsia, severe pre-eclampsia and pre-eclampsia superimposed on essential hypertension showed cytotrophoblastic proliferation in more than 20% of villi where as only half of mild pre-eclampsia cases had this change and none in control. This finding agreed with that of previous workers like Wentworth(1967)¹¹; Fox(1968)¹²;Bhatia et al(1980)¹³; Kher et al(1981)¹⁴ ,Majumdar S et al(2005)¹⁵ and Pasricha N et al(2012)¹⁶, observed that infarcts were always surrounded by a proliferation of cytotrophoblastic cells. So trophoblastic activity serves as a rough guide to the severity of duration of ischemia and its proliferation is a reparative process seen in response to ischaemic damage of placenta.

Sixty five percent of toxemic placentae showed vasculosyncytial membrane deficiency(<5% of villi) well correlated with the observation of Fox(1967)¹⁷, Kher et al(1980)¹⁴,Pasricha N et al(2012)¹⁶ and Narasimaha A et al(2011)¹⁸.Vasculosyncytial membrane represents the principal site of, and are specialised areas for, materno-foetal oxygen transfer. The paucity of vasculosyncytial membrane was seen in higher grade of toxemia correlating with the severity of the disease. The present study observed 70% of toxemic placentae showing high basement membrane counts (>3% of villi in a placentae showed thickened basement membrane) similar observation was reported by Fox(1968)¹²; Sayeed et al(1974)¹⁹; Bhatia et al(1980)¹³; Kher et al(1980)¹⁴;Manjunath HK et al(2012)²⁰ and Narasimha A et al(2011)¹⁸.In this present study 88% of placentae with villous basement-membrane thickening showed cytotrophoblastic cell proliferation almost tallying to the observation of above authors'. Fox (1968)¹² suggested that, cytotrophoblastic cells perhaps secrete basement

membrane substances leading to high basement membrane count. He also suggested that villous basement membrane thickness is a response to placental ischemia as well as due to an immunological reaction. Other villous lesion like increased syncytial knot formation was seen in 82.5% of placentae of toxemia of pregnancy and 20% of control group, similar to the observation of Salvatore(1968)²¹; Sayeed et al(1974)¹⁹; Kher et al (1980)¹⁴; Narasimha A et al(2011)¹⁸; Maham A et al(2012)²² and Manjunatha HK et al(2012)²⁰ Syncytial knot is thought to be a manifestation of degenerative changes in the trophoblastic as well as a reaction to uteroplacental ischemia.

The present study observed 77.5% of cases of toxemia of pregnancy showing fibrinoid necrosis as compared to 20% of control, similar to the observation of Fox(1968)¹²; Sayeed et al (1974)¹⁹; Mirchandani et al(1979)²³ Bhatia et al(1981)¹³; Narasimha A et al(2011)¹⁸; Maham A et al(2012)²² and Pasricha N et al(2012)¹⁶. Fox(1968)¹² has described fibrinoid necrosis in the placental villi not only in toxemia of pregnancy but also significantly in placentae of diabetic, rhesus incompatibility women and in case of premature onset of labour. The aetiology of fibrinoid necrosis is obscure but the possibility that it is due to an immunological reaction within the villous cytotrophoblastic tissue was thought of. Present study found increased incidence of stromal fibrosis in severe pre-eclampsia and eclampsia. Similar observation were also made by Bhatia et al(1981)¹³, Kher et al(1980)¹⁴; Pasricha N(2012)¹⁶; Narasimha A et al(2011)¹⁸. Stromal fibrosis is attributable to decrease foetal perfusion.

V. Conclusion

The foetus, placenta and mother constitute triad of contributors to pregnancy outcome. Placental examination becomes an important but not the only assessment of pregnancy-related problems. The placental examination will help in understanding of the specific aetiologies of adverse outcome which will lead to specific treatment and preventive measures for those with risk for recurrence in subsequent pregnancies specifically in pre-eclampsia and eclampsia cases.

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