

**A COMPARATIVE STUDY OF HISTOPATHOLOGICAL CHANGES IN HUMAN PLACENTAE OF NORMOTENSIVE AND HYPERTENSIVE PREGNANCIES.**

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**ABSTRACT**

**Background:** 5 to 10% of all pregnancies complicated by hypertensive disorders and have great contribution to maternal morbidity and mortality. When maternal health is affected by a medical problem like, hypertension it may also affect the architecture and functions of the placenta. The placenta plays a role of bridge between mother and fetus and considered as a window through which maternal dysfunctions and their impacts on fetal wellbeing can be understood. **Aim and Objective:** To compare histopathological changes in placentae of normal and hypertensive pregnancies. **Material and methods:** 40 placentae were taken from full term pregnant women who had clinically diagnosed hypertension during pregnancy and an equal number of controls were taken. Various histopathological changes in placentae of both groups were recorded and analysed using unpaired 't' test. **Results:** The study showed significantly excessive ( $p < 0.01$ ) syncytial knots, fibrinoid necrosis, villous stromal fibrosis and cytotrophoblastic proliferation in placentae of hypertensive mothers as compared to controls while incidence of vasculo-syncytial membranes of the villi were found significantly less ( $p < 0.01$ ) in placentae of hypertensive mothers. **Conclusion:** Placentae of hypertensive pregnancies showed significant histopathological changes as compared to controls that can be associated with impaired function of placenta, leading to adverse perinatal outcome.

**Key words:** hypertensive pregnancies, normotensive pregnancies, histopathological changes, placentae, pregnancy.

**INTRODUCTION:**

Population based data indicated that approximately 1% of pregnancies are complicated by chronic hypertension, 5-6 % by gestational hypertension (without proteinuria) and 1-2 % by preeclampsia.(1) Gestational

hypertension may results in many serious consequences for both, the mother and the baby. These are associated with vasospasm, pathological vascular lesions in multiple organ systems, increased platelet activation and

subsequent activation of the coagulation system in the microvasculature.(2) The pathological changes are primarily ischemic in nature and affect the placenta, kidney, liver and brain.(3)

Many consider the placenta as pathogenic focus for all manifestations of preeclampsia (the most severe form of hypertensive disorders of pregnancy), because delivery is the only definitive cure for this disease. Early in gestation the spiral arteries (the terminal branches of the uterine artery) are transformed from thick-walled muscular vessels to sac like flaccid vessels, which eventually accommodate a 10-fold increase in uterine blood flow. This transformation involves invasion of the spiral arteries by endovascular trophoblast cells of the placenta. There is evidence that trophoblastic invasion of the uterine spiral arteries is incomplete in women in whom preeclampsia eventually develops. Failure of the spiral arteries to remodel is postulated as the morphological basis for decreased placental perfusion in preeclampsia, which may ultimately lead to early placental hypoxia.(3)

Fetal hypoxia is not uncommon near term and accordingly it may lead to fetal distress and fetal death.(4) In recent years, it has been revealed that there is a clear relationship between confined placental mosaicism and fetal growth retardation.(5)

Variations observed by many authors in histopathological features of placental villi are syncytial knots, fibrinoid necrosis, stromal fibrosis, vasculo-syncytial membrane and cytotrophoblastic proliferation. Syncytial knots are focal aggregation of syncytial nuclei on the outer surface of a tertiary placental villus, forming a multi nucleated protrusion from the villous surface. Such knots are gradually increases in number throughout gestation and at term are present on between 10 and 30% of the

terminal villi. (6) Fibrinoid necroses are small collections of homogenous, eosinophilic material within the villi. At term, placental villi showing fibrinoid necrosis > 3% of placental villi is excessive.(7) Stromal fibrosis is pink coloured collagen fibres within the core of the villi. The stroma of the mature placental villi usually contains little collagen. At term, terminal villi showing stromal fibrosis > 3% of villi is considered as abnormal finding. (8) In mature normal placenta the villous capillaries are sinusoidal and closely approximated to overlying trophoblast. In many villi the dilated capillaries bulge out towards the intervillous space, over such vessels the syncytium is often thinned and may appear to be fused with the vessel wall to form a “vasculo-syncytial membrane” (Fig.4). In mature normal placenta vasculo-syncytial membranes are present in 6-30% of terminal villi. (9) Cytotrophoblastic proliferation can be seen as lighter stained nuclei, present in a single row beneath the syncytiotrophoblast and external to the basement membrane. In mature normal placenta cytotrophoblastic proliferation are present up to 20% of terminal villi. (10)

Placenta is the most accurate record of the infant's perinatal experience. If some time spent on minute examination of placenta after delivery, it provides very useful informations about the perinatal health of the baby and the mother.(11) The present study has been undertaken to compare the histopathological changes in placenta from hypertensive and normotensive mothers.

## **MATERIAL AND METHODS:**

A cross sectional comparative study was carried out from April 2012 to September 2014 in Anatomy department of Sawai Man Singh Medical College, Jaipur (Rajasthan). After obtaining approval from institutional ethical

committee 40 randomly selected mothers with uncomplicated normal pregnancy and equal number with hypertensive mothers were taken from indoor patients of Obstetric and Gynaecology department of S.M.S. Medical College, Jaipur (Rajasthan). The criteria for hypertensive group was systolic blood pressure  $\geq 140$  or diastolic BP  $\geq 90$  mm Hg for first time during pregnancy and for normotensive group was systolic blood pressure  $< 140$  mm Hg and diastolic blood pressure  $< 90$  mm Hg throughout pregnancy.

The age range of the mothers varies from 20 years to 38 years, primipara, gestational age between 37-42 weeks; deliveries by vaginal route were included. While pregnancies with any complication like anaemia, maternal malnutrition, jaundice, multiple pregnancies, placental and systemic disorders which may bring changes in placental histopathology were excluded from study.

After explaining the purpose of study to all respondents, their written consent was taken for study. Complete medical and obstetric history was taken. Then the mothers were examined clinically along with recording of relevant investigation reports to check the inclusion and exclusion criteria. The data was collected using a predesigned proforma.

The placentae were collected soon after delivery and washed in running tap water. Surface dried between blotting papers and the placentae were cut to obtain two samples of size 1cm X 1cm from each placenta, one from peripheral part and one from central part. The pieces were processed for paraffin embedding and sectioning. The slides were stained with Haematoxylin and Eosin stain and examined under light microscope. The histological abnormalities like syncytial knots, fibrinoid necrosis, stromal fibrosis, vasculo-

syncytial membranes and cytotrophoblastic proliferation per 100 villi were recorded. Statistical analysis using unpaired 't' test was done to know significant difference between control and study group if any. P-value  $< 0.05$  was considered as statistically significant. SPSS software version 20.0 was used for all statistical analysis.

## RESULTS:

In the present study, mean villous counts showing syncytial knot formation (Fig.1) were significantly more ( $p < 0.01$ ) in hypertensive group ( $34.38 \pm 7.81$ ) as compared to normotensive group ( $14.25 \pm 6.82$ ). The mean villous counts showing fibrinoid necrosis (Fig.2) were significantly higher ( $p < 0.01$ ) in hypertensive group ( $5.10 \pm 1.82$ ) as compared to normotensive group ( $2.25 \pm 1.66$ ). The mean villous counts showing stromal fibrosis (Fig.3) were more in hypertensive group ( $6.83 \pm 3.92$ ) as compared to normotensive group ( $2.70 \pm 2.63$ ) while the mean villous counts showing vasculo-syncytial membranes (Fig.4) were less in hypertensive group ( $7.28 \pm 4.85$ ) as compared to normotensive group ( $15.78 \pm 6.51$ ) and both these differences were statistically significant ( $p < 0.01$ ). It was observed in the present study that mean villous counts showing cytotrophoblastic proliferation (Fig.5) were again significantly more ( $p < 0.01$ ) in hypertensive group ( $20.75 \pm 9.20$ ) as compared to normotensive group ( $8.70 \pm 5.35$ ).

## DISCUSSION:

The present study showed that the mean numbers of syncytial knots were more in hypertensive group as compared to normotensive group and this difference was highly significant ( $p < 0.01$ ). Similar results were found in earlier studies by Soma et al (1982), Majumdar et al (2005) in Kolkata, Navbir (2012) in Lucknow and Ahmed

and Daver (2013) in Mumbai, where they found significantly more syncytial knots in placentae of hypertensive mothers.(12,13,14,15) The excess of syncytial knot formation in hypertensive pregnancies may also be related to reduced villous blood flow in this condition as there are obliterative changes in the fetal arteries.(16)

The mean numbers of villi showed fibrinoid necrosis were higher in hypertensive group as compared to normotensive group and this difference was highly significant ( $p < 0.01$ ). Similar results were found in earlier studies by Soma et al (1982), Majumdar et al (2005) in Kolkata, Romero et al (2008) in Spain, Navbir (2012) in Lucknow, where they found significantly more fibrinoid necrosis in placentae of hypertensive mothers.(12,13,14,17) Fibrinoid necrosis is the hallmark of immunological reaction in the villous tissue. It has been claimed that anti-trophoblast antibodies may be found in the serum of pregnant women (Hulka and Brinton 1963; Wilkon 1963a) and the levels of this antibody are unduly high in the serum of the patients suffering from preeclampsia. It is possible that in both normal and preeclamptic pregnancies an antibody-antigen reaction occurs in the trophoblast.(18)

Statistically highly significant ( $p < 0.01$ ) difference was observed in the mean numbers of villi showed stromal fibrosis and was more in hypertensive group as compared to normotensive group. Similar results were found in earlier studies by Majumdar et al (2005) in Kolkata, Navbir (2012) in Lucknow, where they found significantly more stromal fibrosis in placentae of hypertensive mothers. Villous fibrosis is associated with reduced fetal villous blood flow.(13,14) The high incidence of villous fibrosis in the placentae from hypertensive women is probably due to reduction of fetal blood flow by obliterative endarteritis of fetal

stem arteries, which is a common feature of such placentae.(19)

The mean numbers of villi showed vasculo-syncytial membranes were less in hypertensive group as compared to normotensive group and this difference was highly significant ( $p < 0.01$ ). Similar results were found in earlier studies by Navbir (2012) in Lucknow and Ansari et al (2011) in Aligarh, where they found significantly less vasculo-syncytial membranes in hypertensive group.(14,20) A low (less than 6%) vasculo-syncytial membrane count is an indication of either immaturity or regression.(21) The cytotrophoblastic proliferation showing villi were more in hypertensive group and this difference was highly significant ( $p < 0.01$ ). Similar results were found in earlier studies by Soma et al (1982), Majumdar et al (2005) in Kolkata, Romero et al (2008) in Spain, Navbir (2012) in Lucknow and Ahmed and Daver (2013) in Mumbai, where they found significantly more syncytial knots in placentae of diabetic mothers.(12,13,14,15,17)

## CONCLUSION:

The study has conclusively shown that placentae of hypertensive mothers show significant histopathological changes that can be associated with impaired function of placenta, leading to adverse perinatal outcome.

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**Table 1: Histological changes of placentae in hypertensive and normotensive pregnancies**

Parameter	Hypertensive pregnancies N=40 (Mean ± SD)	Normotensive Pregnancies N=40 (Mean ± SD)	't' value	P-value*
<b>Syncytial knots</b>	34.38 ± 7.81	14.25 ± 6.82	12.279	< 0.001
<b>Fibrinoid necrosis</b>	5.10 ± 1.82	2.25 ± 1.66	7.317	< 0.001
<b>Stromal fibrosis</b>	6.83 ± 3.92	2.70 ± 2.63	5.533	< 0.001
<b>Vasculo-syncytial membrane</b>	7.28 ± 4.85	15.78 ± 6.51	6.622	< 0.001
<b>Cytotrophoblastic proliferation</b>	20.75 ± 9.20	8.70 ± 5.35	7.161	< 0.001

SD – Standard deviation \* Unpaired 't' test

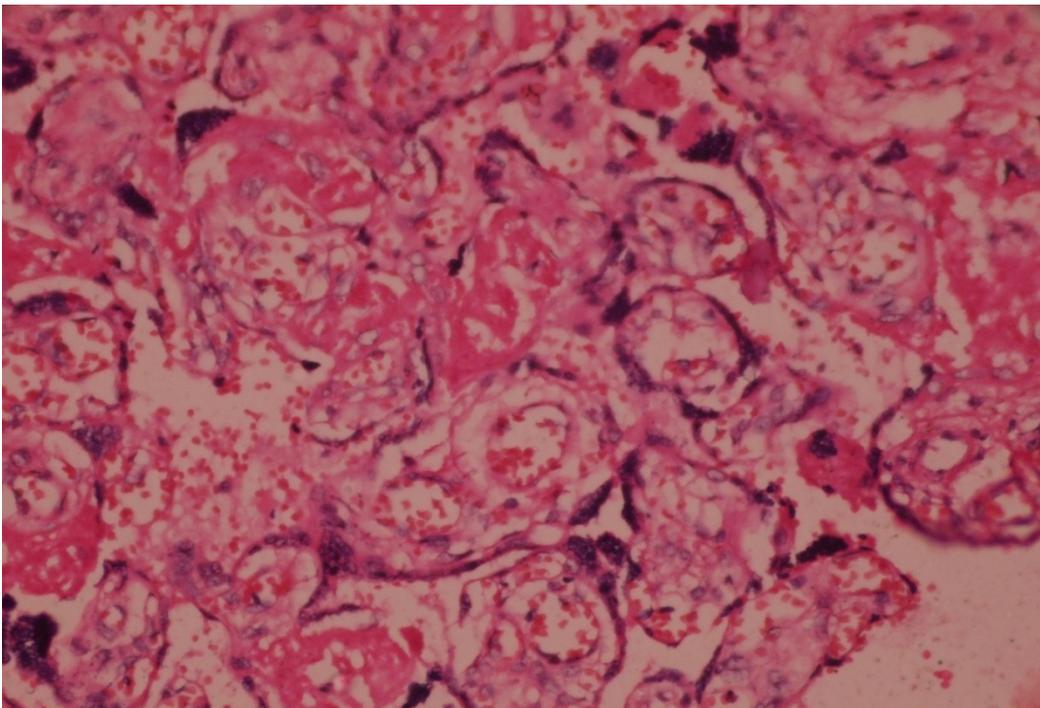


Figure 1: Syncytial knots in study group (Haematoxylin and Eosin group, 40X)

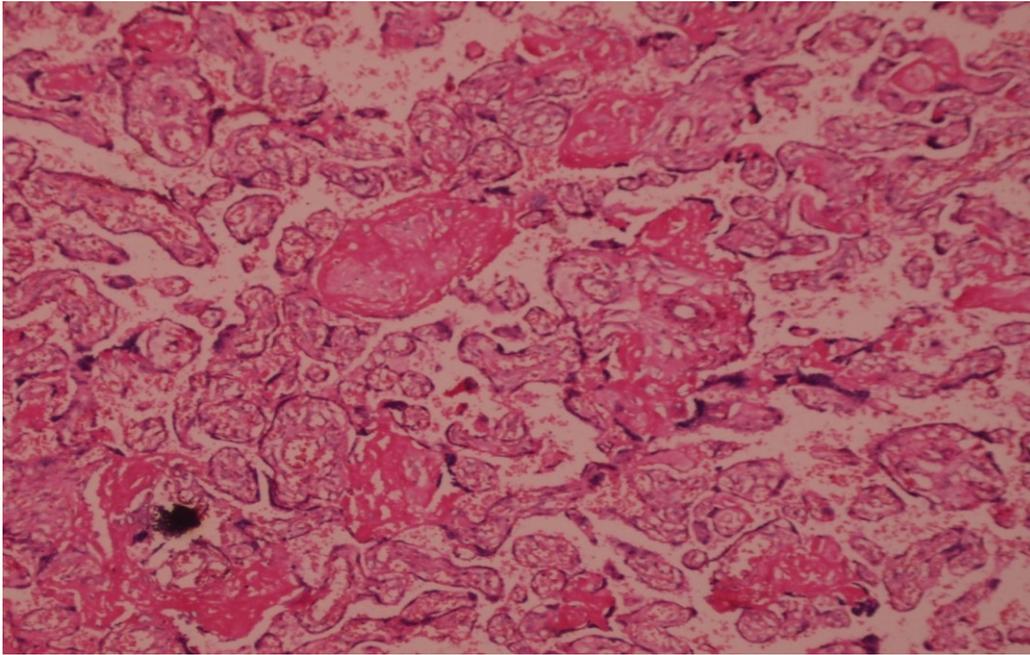


Figure 2: Fibrinoid necrosis in study group (Haematoxylin and Eosin group, 40X)

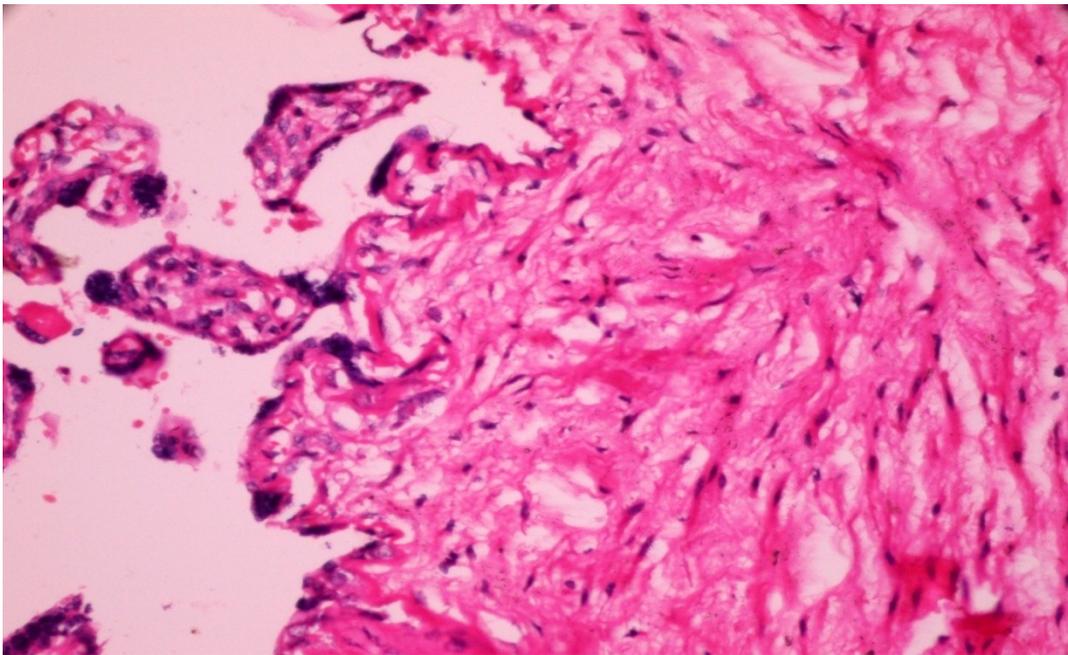


Figure 3: Stromal fibrosis in study group (Haematoxylin and Eosin group, 40X)

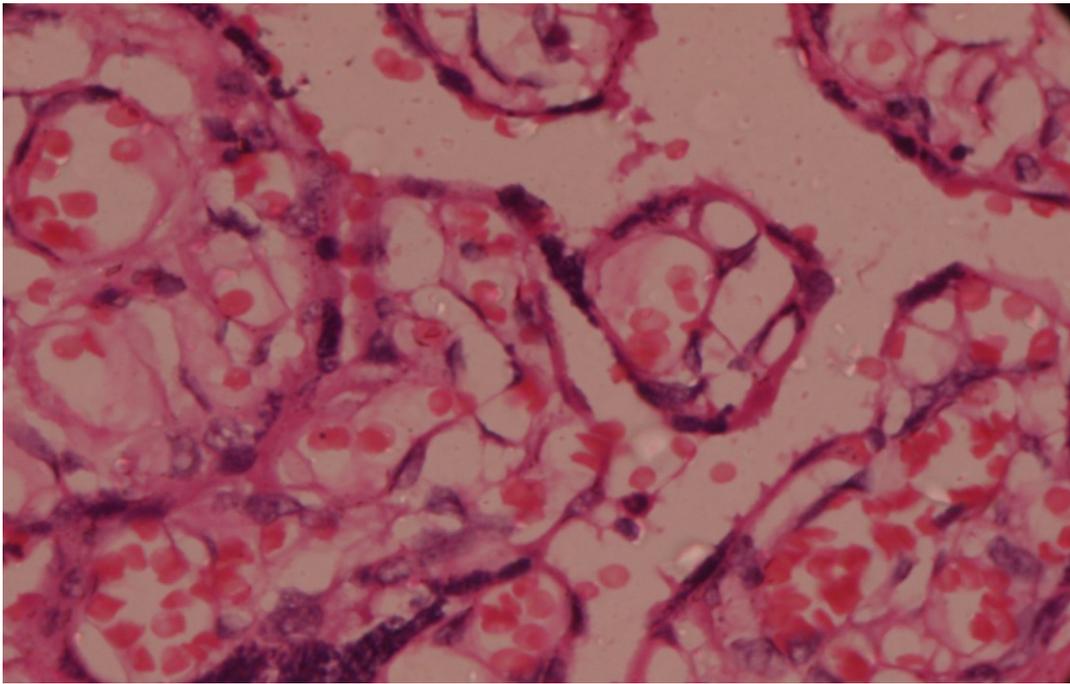


Figure 4: Vasculo-syncytial membrane in control group (Haematoxylin and Eosin group, 100X)

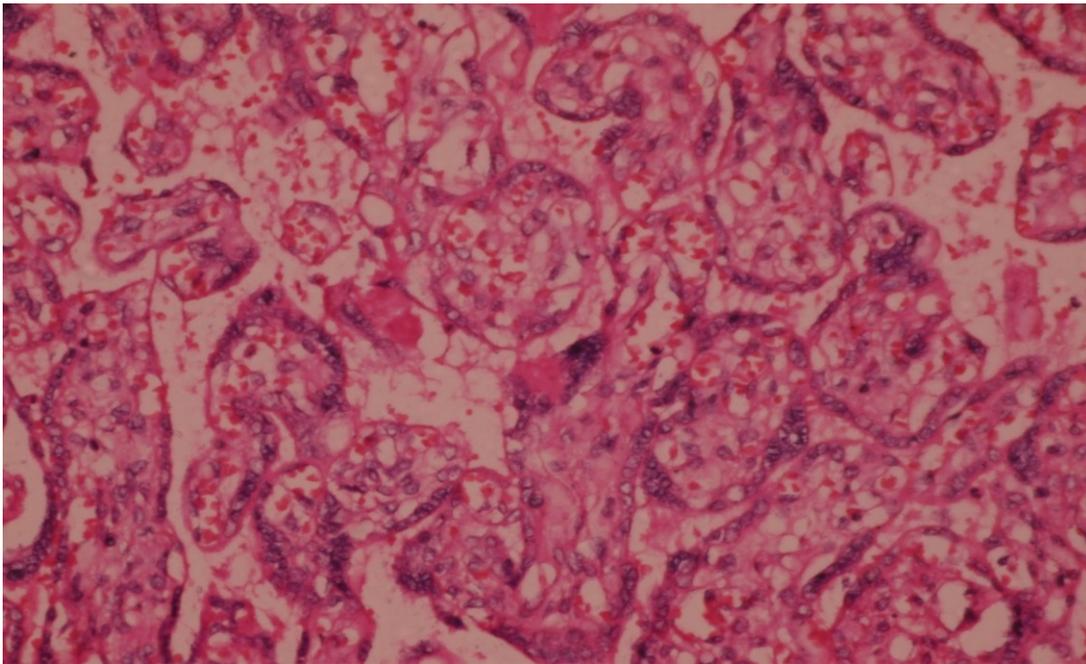


Figure 5: Cytotrophoblastic proliferation in study group (Haematoxylin and Eosin group, 40X)