EFFECTS OF PREGNANCY INDUCED HYPERTENSION ON HUMAN PLACENTA

Rohini Motwani[1], Yogesh Sontakke[2], Meena Goyal[3]

HOW TO CITE THIS ARTICLE:
Rohini Motwani, Yogesh Sontakke, Meena Goyal. "Effects of pregnancy induced hypertension on human placenta". Journal of Evolution of Medical and Dental Sciences 2013; Vol2, Issue 33, August 19; Page: 6275-6282.

ABSTRACT: INTRODUCTION: Placenta is a unique organ which arise de novo, directly related to the growth and development of the foetus in the uterus. A thorough examination of the placenta in-utero, as well as post-partum, gives valuable information about the state of the foetal well being. Pregnancy Induced Hypertension is a well recognized obstetric hazard and observed more frequently in developing countries. **OBJECTIVES**: The present study was undertaken to analyze placental changes in the pregnancy induced hypertension. **MATERIAL AND METHODS**: thirty placentae of mothers with uncomplicated pregnancy as control group and thirty with pregnancy induced hypertension as study group were studied with gross examination and histologically. **RESULTS**: Gross examination revealed presence of smaller placentae with foci of calcification and infarction in study group. On light microscopic examination, the striking villous abnormalities were observed in the study group which included increased Syncytial knots formation, fibrinoid necrosis, stromal fibrosis, hyalinized villi, altered villous vascularity (hypo vascularity), cytotrophoblastic cell proliferation, endarteritis obliterans, intervillous haemorrhage and basement membrane thickening. **CONCLUSIONS**: Pregnancy induced hypertension immensely affected placenta which may be responsible for wore postnatal outcomes. This study is of particular importance for Pathologists, Embryologists and Gynaecologists.

KEYWORDS: placenta, pregnancy induced hypertension, chorionic villi.

INTRODUCTION: The placenta is a distinctive characteristic of higher mammals which is attached to the uterus and is connected to the foetus through the umbilical cord. It is often disposed soon after parturition without adequate examination though the researchers have emphasized the benefits associated with the anatomical examination of the placenta. As being an organ of the vital importance for the continuation of a pregnancy and fetal nutrition, it has evoked great interest among the anatomists, pathologists and the obstetricians [1]. The information provided from the pathological assessment of the placenta may provide important clinical information of both the mother and the neonate. Placenta also represents the only point of contact between maternal and foetal tissues and plays a dominant role in the immunological acceptance by the mother of the foetal graft [2, 3].

Hypertension is one of the common complications met with in pregnancy and contributes significantly to maternal and perinatal morbidity and mortality. It is a sign of an underlying pathology which may be pre-existing or appears for the first time during pregnancy. To prevent complications, it is obligatory to care properly the patients in pre-eclamptic condition, ie, pregnancy-induced hypertension (PIH). PIH is characterized by blood pressure elevation after 20 weeks of gestation that is often accompanied by proteinuria [4]. In developing nations, the incidence of the

PIH is reported to be 4-18%, with hypertensive disorders being the second most common obstetric cause of stillbirths and early neonatal deaths in these countries. Several important findings have contributed to our understanding of maternal genetic predisposition, eg, specific patterns of genetic variant of angiotensinogen gene and quantitative trait loci on some chromosomes including 5q, 10q, and 13q [5,6]. Both background and progression course of PIH vary among cases, and it is difficult to predict whether the condition is improved in response to treatment or is aggravated and resulted in preterm termination. Currently, the onset of PIH is considered to depend not only on a sole or a few pathological events. It may rather be triggered by a load of predisposing factors that potentially promote circulatory dysfunction [7]. Placental perfusion is maintained by two distinct cardiovascular systems, ie, maternal blood flow and fetal circulation. Therefore, pathophysiology of the placenta is closely associated with both maternal status and fetal development. Pregnancies complicated with hypertension or other disorders are reflected in the placenta in a significant way (both macroscopically and microscopically). The identification of the clinical entity and effective management play a significant role in the outcome of pregnancy, both for the mother and the baby. The aim of the present study was to appreciate qualitatively and to assess quantitatively the pathological features of placentas associated with pregnancy induced hypertension (PIH)

MATERIALS AND METHOD: For the present study sixty full term placentae were taken from mothers who delivered either vaginally or by caesarian section, from the Department of Obstetrics and Gynaecology of tertiary care hospital. Out of these, thirty placentae were of mothers with uncomplicated pregnancy (control group) and thirty were placentae of patients (Study group) who had blood pressure recording of 140/90 mm of Hg or more, with or without oedema and/or proteinuria (inclusion criteria) without having antecedent history or any documentation of hypertension prior to pregnancy. In both groups, mothers were examined clinically (for height, weight, blood pressure, pulse, anaemia, jaundice etc.) along with recording of their medical history (history of past illness, history of previous child birth, etc). An exclusion criterion was any abnormalities in blood sugar, blood urea, serum bilirubin and creatinine, haemoglobin levels for both the groups.

The placentae were collected soon after the delivery and cleaned keeping one centimetre long umbilical cord. Weights of the placentae were noted. Perfusion of placentae with 10% formalin through umbilical vessels was followed by immersion in a jar containing 10% formalin for 48 hours. Gross examination of the placentae for presence of any infarction, calcification and retro placental clots was done. Tissues each of 2×2 cm were taken from placentae and processed for histological observations for light microscopic studies. Tissues were taken from histological assessment from site near the attachment of umbilical cord, margin and centre of the placenta. It was also examined for the presence of calcified and infracted area if any. Slides were stained with Haematoxylin and Eosin (H & E) for general scrutiny and to study the histology of placenta. Slides were also assessed using Masson's Trichrome for fibrosis. In light microscopic examination of the placental villi were screened for counting of number of syncytial knots per 100 villi, fibrinoid necrosis, stromal fibrosis, medial coat proliferation of foetal blood vessels, intervillous haemorrhage, cytotrophoblastic cellular proliferation and calcification.

RESULTS: In the present study, mean weight of the placenta was significantly lower in PIH groups (395.00 gms) than in the control group (462.16 gms) [Table 1]. On the gross examination of the placentae, calcification was found more common in placentae of PIH cases (70%) than that of control group (26.66%). The areas of infarction in placentae of control group (3%) were observed significantly less than that in the PIH cases (43.33 %) [Table 1].

Light microscopic examination of the placental villi showed significant changes in the study group. The number of areas of Syncytial knots in PIH group (70.36/100 villi) was significantly increased than in control group (26.93/100 villi) [Fig-1]. Villous vascularity was found to be higher in control group as compared to PIH. The number of areas of fibrinoid necrosis in PIH group (11.83/ 100 villi) was also found to be increased than in control group (3.73/100 villi) [Fig-2A]. Stromal fibrosis and medial coat proliferation of foetal blood vessels were also increased in PIH group (66.66% and 73.33% cases) than that in control group (23.33% and 10% cases respectively) [Fig-2B & 3A]. Intervillous haemorrhage was absent in control group but observed in more than half of the PIH cases (56.66%) [Fig-3B]. Hyalinized villi and calcification were found more commonly in PIH group (46.66% and 73.33% cases) than that in control group (36.66% and 36.66% cases respectively). The mean area of cytotrophoblastic proliferation was more in PIH group (4.19) than in control group (3.46) [Table 1].

DISCUSSION: The placenta has been described as the mirror of the perinatal mortality. Evaluation of placenta is very important in high risk pregnancies because the neonatal outcome depends upon the status, growth, and development of placenta. The chorionic villi are the functional unit of placenta and provide oxygen & nourishment to foetus & also serve as excretory unit [8]. A glance at the literature reveals that the PIH exerts its deleterious effects on the placenta. So, the present study was undertaken to analyze placental changes in the PIH cases with a view to assess the significance of villous abnormalities by histopathological methods under light microscopy because these changes may serve as a guide to the duration and severity of disease [9]. Wide spectrum of villous lesions was observed in toxaemic cases in our study. The villous lesions could be attributed to the decreased maternal utero-placental blood flow in preeclampsia due to maternal vasospasm as proposed by Browne and Veall [10]. Damania KR et al found that placental pathology worsens with progressive increase in hypertension [11].

In the present study we observed that mean weight of placenta was significantly lower ($p > 0.01$) in the hypertensive group than in the control group which is due to placental insufficiency [11, 12, 13]. In earlier reports as well as in the present study, the gross examination of the placentae from PIH mothers showed higher incidence of calcification and infarction [14]. The calcification indicates an 'aging' of the placenta that occurs near the end of pregnancy. But it may be the sign of the premature aging in these cases of PIH, which will decrease the amount of nutrition and oxygen going to the baby and may worsen the postnatal outcome. Placental infarction of more than 5% surface area is considered pathological and more frequently seen in toxaemia due to thrombotic occlusion of maternal uteroplacental vessels [15, 16].

Syncytial knots are consistently present, increasing with increasing gestational age, and can be used to evaluate villous maturity. Increased Syncytial knots are associated with conditions of uteroplacental malperfusion and are important in placental examination [17]. Heazella AEP et al

reported increased numbers of syncytial knots in placentae of pregnancies complicated by pre-eclampsia and foetal growth restriction (FGR) [18]. They hypothesized that the formation of syncytial knots may be induced by exposure to hypoxia. Fibrinoid necrosis is seen as a nodular mass of homogenous acidophilic material in the villi. Fibrinoid necrosis has been considered as a hallmark of an immunological reactions within the trophoblastic tissue [9]. In the present study, the fibrinoid necrosis per 100 villi was significantly higher in PIH group in comparison to the control group ($p < 0.05$) which corresponds with the study of earlier researchers [18, 19]. Fibrinoid necrosis may be a manifestation of endothelial damage in the placenta which may lead to increased coagulation tendency [18, 19].

Obliterative endarteritis of the fetal stem arteries is characterized by swelling and proliferation of intimal cells, together with thickening and reduplication of the basement membrane. In the present study, stromal fibrosis and medial coat proliferation of foetal blood vessels were also increased in PIH group which corresponds with the study of Masodkar AR and Narasimha A et al [18, 19, 20]. This increased incidence of stromal fibrosis may be related to reduce uteroplacental blood flow as a result of obliterative endarteritis which was found in placentae of PIH group [14]. Intervillous haemorrhage was also observed in placentae of PIH group as by Narasimha A et al [20]. There was significant increase in calcification in placentae of PIH group. Calcification is regarded as evidence of placental senescence or degeneration [8]. As reported in other studies as well as in our study villus vascularity was lower in PIH group [17, 18, 20]. The reduced number of vessels may be due to their de-novo poor formation or secondary to fibrosis [21]. Cytotrophoblastic cellular proliferation was significantly higher in PIH group [14, 20] which appears in response to hypoxia as seen in conditions associated with reduced maternal blood flow. Basement membrane thickening is the by product of cytotrophoblastic cell hyperplasia as the basement membrane protein is secreted by these cells which was observed in severe cases of PIH [22]. All the above changes in the placentae of PIH cases may be due to reduced utero-placental blood flow, which are accountable for increase in maternal and foetal mortality and morbidity. This signifies the need of infinitesimal assessment of placenta at the time of delivery.

CONCLUSION: The gross abnormalities and villous lesions in the PIH group were significant. Further studies have to be undertaken to ascertain the statistical significance of microscopic villous abnormalities among eclamptic patients. Pregnancy Induced Hypertension alters the placental histomorphology. To avoid the placental malformation, prompt treatment of these cases is required.

REFERENCES:

1. Nobis P, Das U (1990). Placental morphology in hypertensive pregnancy. Jr Obstet Gynecol 40:166-9.
2. Morgan RP (2003). Immunology of term and preterm labor: Reproductive biol and endocrinol 1:122.
3. Errol RN, Danny JS, Susan JF (2001). Implantation and survival of early pregnancy. N Engl J Med 345:1400-8.
4. National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy (2000). Report. Am J Obstet Gynecol, 183: S1–S22.

5. Van Dijk M, Mulders J, Poutsma A (2005). Maternal segregation of the Dutch preeclampsia locus at 10q22 with a new member of the winged helix gene family. Nat Genet 37:514–9.
6. Johnson MP, Fitzpatrick E, Dyer TD (2007). Identification of two novel quantitative trait loci for pre-eclampsia susceptibility on chromosomes 5q and 13q using a variance components-based linkage approach. Mol Hum Reprod 13:61–7.
7. Redman CW, Sargent IL (2005). Latest advances in understanding preeclampsia. Science 308:1592–4.
8. Fox H (1970). Effect of hypoxia and trophoblast in organ culture. Am J Obs Gynaecol 107: 1058-1064.
9. Fox H. Pathology of Placenta.2nd ed. Philadelphia; W.B Saunders: 1997, pp 1- 39.
10. Browne JCM, Veall N (1953). The maternal blood flow in normotensive and hypertensive women. J Obst Gynaecol of British Empire 60:141-7.
11. Damania KR, Salvi VS, Ratnaparki SK, Daftari SN (1989). The placenta in hypertensive disorder in pregnancy. J Obst and Gynaecol Ind 39:28-31.
12. Kalousek DK, Langlosis S. The effects of placental and somatic chromosomal mosaicism on foetal growth. In: Ward RHT, Smith SK, Donnai (eds), Early foetal growth and development, RCOG Press,1994, pp-245-56.
13. Palaskar A, Chaudhary KR, Mayadeo NM (2001). Foeto-placental weight relationship in normal pregnancy and pre-eclampsia-eclampsia. Bombay hospital journal 43(3):361-3.
14. Majumdar S, Dasgupta H, Bhattacharya K, Bhattacharya A (2005). A Study of Placenta in Normal and Hypertensive Pregnancies. J Anat society India 54 (2):34-8.
15. Zeek PM, Assali NS (1950). Vascular changes in the decidua associated with eclamptogenic toxaemia of pregnancy. Am J Clin Pathol 20: 1099-109.
16. Kher AV, Zawar MP (1981). Study of placental pathology in toxemia of pregnancy and its foetal implications. Indian J Pathol Microbiol 24:245-51.
17. Sodhi S, Mohan H, Jaiswal TS, Mohan PS, Rathee S (1990). Placental pathology in Pre-eclampsia syndrome. Indian Jr of patho and microbio 33 (1):11-6
18. Kristina L, Raanan S, Rebecca B (2009). Syncytial knots as a Reflection of Placental Maturity: Reference values for 20 to 40 weeks gestational age. Pediatric and Developmental Pathology 28:28-37.
19. Heazella AEP, Moll SJ, Jones CJ, Baker PN, Crocker IP (2007). Formation of syncytial knots is increased by hyperoxia, hypoxia and reactive oxygen species. Placenta 28 (Suppl A):33-40.
20. Masodkar AR, Kalamkar LR, Patke PS (1985). Histopathology of placenta and its correlation with fetal outcome. Jr Obstet Gynae of India 35:294-7.
21. Narasimha A, Vasudeva DS (2011). Spectrum of changes in placenta in toxemia of pregnancy. Indian J Pathol Microbiol 54:15-20.
22. Sodhi S, Mohan H, Jaiswal TS, Mohan PS, Rathee S (1990). Placental pathology in Pre-eclampsia syndrome. Indian Jr of patho and microbio 33 (1):11-6.

Table 1: Comparative analysis of Histomorphology of placenta from the Control and PIH mothers

Parameters#	Control group (N = 30)	PIH group (N = 30)
Placental weight (gms)*	462.16 ± 66.27	395.00 ± 63.39
Areas of calcification$	08 (26.66%)	21 (70.00%)
Mean areas of infarction$	01 (03%)	13 (43.33%)
Syncytial knots per 100 villi*	26.93 ± 10.49	70.36 ± 13.34
Villous vascularity	9.62 ± 1.64	4.91 ± 0.89
Fibrinoid necrosis*	3.73 ± 1.99	11.83 ± 4.3
Stromal fibrosis$	07 (23.33%)	20 (66.66%)
Medial coat proliferation$	03 (10.00%)	22 (73.33%)
Intervillous haemorrhage$	00	17 (56.66%)
Hyalinised areas$	04 (13.33%)	14 (46.66%)
Calcification$	11 (36.66%)	22 (73.33%)
Cytotrophoblastic cellular proliferation*	3.46 ± 1.04	4.19 ± 1.15

* unpaired‘t’ test was applied for these parameters

$ Chi-square test was applied for these parameters

Change is considered to be significant if p value is < 0.05

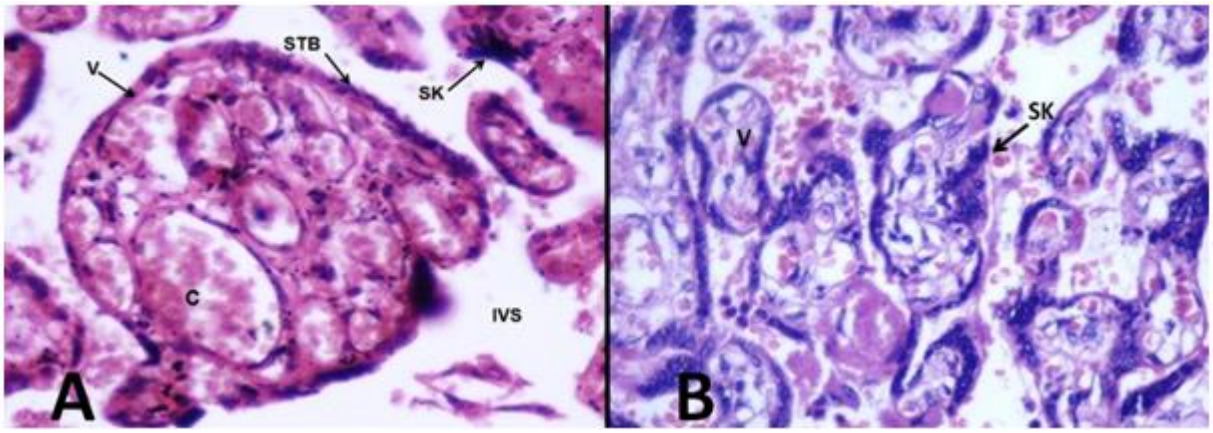

Figure 1: Histology of Placenta. (H & E Stain, X400). A: Placenta from Control group with well vascularised chorionic villi and only few syncytial knots. B: Placenta from PIH mothers showing increased syncytial knots. V: chorionic villi, SK: syncytial knots, STB: syncytiotrophoblast; IVS: intervillus space; C: capillary

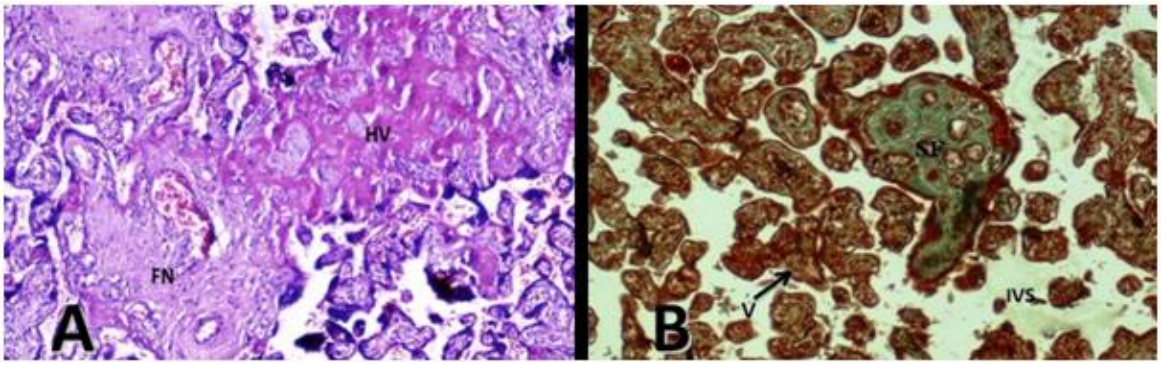

Figure 2: Placenta from PIH mothers. A: Placenta showing areas of fibrinoid necrosis and hyalinized villi (H&E stain, X100). B. Placenta showing villous fibrosis. (Masson's trichrome stain, X100). V: villus, FN: Fibrinoid necrosis, HV: Hyalinized villi, SF: Stromal fibrosis, IVS: Intervillous space.

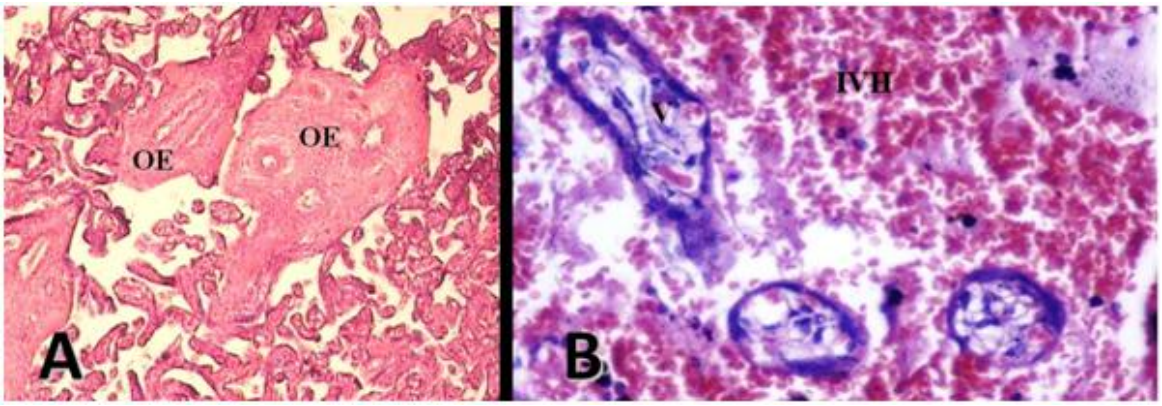

Figure 3: Placenta from PIH mothers. A. Placenta showing obliterative endarteritis of foetal blood vessels (H & E stain, 10X). B: Placenta showing intervillous haemorrhage (H & E stain, 40X). IVS: intervillous space; V: villus; OE: obliterative endarteritis; IVH: intervillous haemorrhage.

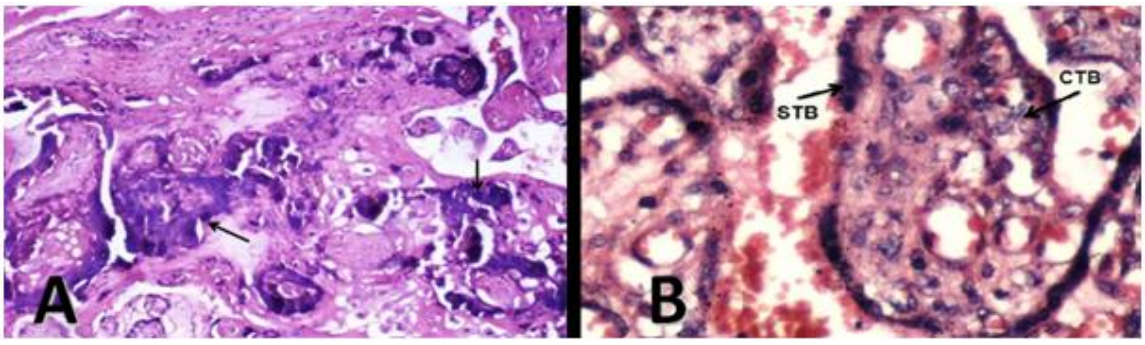

Figure 4: Placenta from PIH mothers. A. Placenta showing calcification (arrows) (H & E stain, 10X). B: Placenta showing Cytotrophoblastic proliferation (H & E stain, 40X). STB: Syncytiotrophoblast; CTB: Cytotrophoblast

AUTHORS:

1. Rohini Motwani
2. Yogesh Sontakke
3. Meena Goyal

PARTICULARS OF CONTRIBUTORS:

1. Senior Resident, Department of Anatomy, All India Institute of Medical Sciences, New Delhi.
2. Assistant Professor, Department of Anatomy, Sri Aurobindo Medical College and Post Graduate Institute, Indore, MP.
3. Professor, Department of Anatomy, Pt. J.N.M. Medical College, Raipur, Chhattisgarh.

NAME ADRRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Yogesh Sontakke,
Department of Anatomy,
SAIMS Medical College and Post Graduate Institute,
Indore – 453555, MP, India.
Email – dryogesha@rediffmail.com

Date of Submission: 03/08/2013.
Date of Peer Review: 04/08/2013.
Date of Acceptance: 07/08/2013.
Date of Publishing: 17/08/2013.