

## Histological Changes in Placenta in Hypertensive Pregnancy & its relation to birth weight of Baby

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**Abstract:** The placenta is an organ that connects the developing fetus to the uterine wall to allow nutrient uptake, waste elimination, and gas exchange via the mother's blood supply. Placentae are a defining characteristic of eutherian or "placental" mammals, but are also found in some snakes and lizards with varying levels of development up to mammalian levels. The study was conducted in the Department of Anatomy, in Gauhati Medical College and Hospital. The material for the study, which consisted of 103 human placentae, was collected from the Labour Room of the Department of Obstetrics and Gynaecology of the same institution from a period between 01/06/2010 to 31/08/2011. Histological findings like hypermature villi, stromal fibrosis and syncytial knots are seen in higher range in eclampsia whereas decidual haematoma, obliterative endarteritis and fibrin deposition are more in preeclampsia cases. The average birth weight of baby is comparatively lower in hypertensive group but difference in weight in both control and study group is not statistically significant i.e.  $p > 0.05$ . A low ratio of weight of baby to weight of placenta is evident in pregnancy induced hypertension from the study. The relationship between both groups would have been more conclusive if more cases would have been available for study with detailed clinical correlation.

**Keywords:** Placenta, Hypertensive Pregnancy.

**INTRODUCTION**

The placenta is an organ that connects the developing fetus to the uterine wall to allow nutrient uptake, waste elimination, and gas exchange via the mother's blood supply.

Placentae are a defining characteristic of eutherian or "placental" mammals, but are also found in some snakes and lizards with varying levels of development up to mammalian levels [1]. The word placenta comes from the Latin for cake, from Greek plakoenta/plakounta, meaning "flat, slab-like", in reference to its round, flat appearance in humans. Prototherial (egg-laying) and metatherial (marsupial) mammals produce a choriovitelline placenta that, while connected to the uterine wall, provides nutrients mainly derived from the egg sac [2, 3]. The placenta develops from the same sperm and egg cells that form the fetus, and functions as a fetomaternal organ with two components, the fetal part (Chorion frondosum), and the maternal part (Decidua basalis).

The knowledge of the 'After birth', which also includes the placenta, goes far back into human history and reference to it is to be found in many ancient literatures including the Old Testament. In classical Greek literature also, three fetal membranes i.e. the chorion, the amnion and the allantois were recognized

and named. Of course the placenta is a only specialized portion of fetal membranes [4, 5].

However, until the early 16<sup>th</sup> century, a time of renaissance of Anatomy, no proper scientific basis could be established regarding placental functions. In 1564, Arantius found that there was a continuity between fetal and maternal vascular system. In 1651, Harvey studied the fetal arterial and venous circulation of placenta. Later John Mayow in 1643 – 1679 described the nature of uteroplacental circulation. In 17<sup>th</sup> century, scientist threw light in to the structure and function of placenta [6].

**MATERIALS AND METHODS**

The study was conducted in the Department of Anatomy, in Gauhati Medical College and Hospital. The material for the study, which consisted of 103 human placentae was collected from the Labour Room of the Department of Obstetrics and Gynaecology of the same institution from a period between 01/06/2010 to 31/08/2011.

### **Selection of cases**

For collection of placentae for this study, pregnant women with hypertension admitted in Obstetrics and Gynaecology department were selected. Those women between 18 to 35 years of age with a gestational age of the fetus between 37 to 42 weeks were examined. Both primigravida and multigravida of average height and weight upto 4<sup>th</sup> parity were taken in the study. The gestational period was calculated using Naegele's Rule, by adding nine calendar months and seven days to the date of last menstrual period (LMP).

At first a detailed history of the patient was taken regarding the presence or absence of any medical or obstetrics disease before and during pregnancy. The patients giving history of any systemic disease before pregnancy, those patients who developed any medical or obstetrics problem during pregnancy other than hypertension and patients who failed to give a precise account of last menstrual period were excluded from the study. Thus, only those cases developing hypertension during pregnancy, i.e. Pregnancy Induced Hypertension (PIH) with a live born baby were selected as cases for this study. However patients without any problem both before and during pregnancy and giving birth to live born babies only were also selected for this study as control group for comparative analysis.

### **Sectioning of placenta, tissue sampling and fixation**

The Placenta was immersed in a large jar containing 10% formal saline as soon as possible for 24 hours. The next day it was transferred to another jar containing 10% formal saline and kept for 7 days for "better fixation and histological results" [7]. According to Novak and Woodruff, 1979 [8] the colour change is best appreciated if the placenta is fixed for at least a week in formalin before slicing into thin sections. Further they are of opinion that changes in the syncytium are difficult to appreciate if the tissue is not uniformly fixed and preserved. To check for any abnormality inside, the placenta was cut with a scalpel into pieces for direct observation.

As a routine procedure the full thickness samples were taken, one from the central area little away from the cord, one piece from the marginal area irrespective of whether the areas are normally looking or not and from the mid region. The sectioning done for sampling was cut to about 1cm X 1.5 cm X full thickness of the placenta. The tissue thus obtained were kept in 10% formal saline in small containers which were labeled to keep track of the details of the placenta from which the blocks were obtained. After 24 hours, the tissues were processed for staining.

### **Processing and staining:**

The procedure for paraffin block preparation was followed as is usually done for Haematoxylin and Eosin staining in the histology section of the Anatomy Department of Guwahati Medical College and Hospital.

The tissue blocks were dehydrated with ascending grades of alcohol, cleared with xylene, and embedded in melted paraffin and finally paraffin blocks were prepared [9]. From the paraffin blocks several micro sections ranging from 4-6 microns were made in Minot's Rotary Microtome.

These sections were mounted on a clean glass slide and further processed for staining. This H & E staining for examination of placenta was highly preferred by Benjamin Tenny [10] and Morrison J E [11]. And these slides were stained by Haematoxylin and Eosin as per standard Laboratory method [12]. The stained sections were covered with a coverslip and observed under the microscope – first under low power and then under higher magnification with oil emersion objective and relevant high power fields were recorded by photography.

The following features were emphasized upon microscopically:

1. Villi – premature / mature / hypermature
2. Intervillous space
3. Syncytial knots
4. Fibrin deposition
5. Stromal fibrosis
6. Villous fibrosis
7. Endarteritis obliterans

## **REVIEW OF LITERATURE**

### **Definition of placenta**

Mossman [13] defined the placenta as an apposition or fusion of the foetal membranes to the uterine mucosa for physiological exchange. The gross and microscopic changes in the placenta are so poorly understood that it becomes difficult to define adequately how a normal placenta looks.

Hamilton and Boyd [7] observed that owing to its great structural variability, not only from species to species, but also in a given species, the placenta is very difficult to define. It was customary to consider this organ as a part of the "afterbirth" along with other ancillary structures of mammalian conceptus which do not become part of the neonate. Realdus Columbus in the first edition of his book, *De Re Anatomica* used the term "Placenta" for the first time.

The human placenta is classified as chorio-allantoic since it is vascularized by vessel homologous with the allantoic vessels of the lower mammals. The term "chorion" was used by Galen. Again it is haemochorial because of the nature of its membrane; deciduate because along with the delivery of the placenta, maternal decidua is shed along with it; discoidal because of its circular shape; and villous because of its villi.

### **Development of placenta**

By the end of third week, the anatomical arrangements necessary for physiological exchanges between the mother and her embryo are established. A complex vascular network is established in the placenta by the end of fourth week, which facilitates maternal-embryonic exchanges of gas, nutrients and metabolic waste products.

The placenta is a foetomaternal organ that has two components:

- A fetal part that develops from chorionic sac
- A maternal part that is derived from the endometrium

The central feature of reproduction is the fusion of male and female pronuclei at fertilization. Fertilization normally occurs in the ampullary region of the uterine tube within 24 hours of ovulation. When the mature ovum develops into a zygote a diploid cell with 46 chromosomes is formed. Fertilized oocyte undergoes segmentation or cleavage which distribute the cytoplasm approximately equally among daughter blastomeres. Once eight cells have formed, a process of compaction occurs. This process is important for generation of cell diversity in early embryo.

### **Microscopic structure of placenta**

Chorionic villi are structural unit of placenta and are usually classified into two types, anchoring and free or floating villi. Their trophoblastic covering layers consists of two layers - it's the syncytial layer which forms the epithelial covering of the villi and the cytotrophoblastic layer which represent a germinative population [14]. The cells of trophoblast which are frequently called Langhans cells gradually decrease in number and tend to be inconspicuous and flattened between the syncytiotrophoblast and the basement membrane [15].

Syncytial knots are present, which are actually aggregation of degenerative nuclei, and represent a sequestration phenomenon by which senescent nuclear material is removed from adjacent metabolically active area of syncytium.

The cells of cytotrophoblast are pale staining with slight basophilia. In earlier stages, the cytotrophoblasts forms an almost continuous layer on the basal lamina. After 4<sup>th</sup> month it gradually expands itself producing syncytium, which comes to lie on the basal lamina over an increasingly large area (80% at term), and becomes progressively thinner [16].

Fibrinoid deposits are frequently found on the villous surface in areas lacking

syncytiotrophoblast. They may constitute a repair mechanism in which fibrinoid deposits forms a wound surface that is subsequently re-epithelialized by trophoblast [17].

### **Placental changes and PIH**

The placenta is a documentation of events of the gestational life of the foetus. Normally the placental morphology varies considerably during its short life span. Alteration in placenta as part of "Aging" phenomenon are probably a part of maturation process and go hand in hand with continued growth of placenta. Fox [18] has stressed the importance of analyzing the placental pathology quantitatively and has stated that the importance of lesions could be realized only when assessed in relation to foetal growth and maturation.

Pregnancy complications like hypertension, gestational diabetes, anaemia etc. are reflected in the placenta in a significant way. 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 [19]. Thus, after delivery if the placenta is examined minutely it provides much insight into the prenatal health of the baby and mother. For this reason an anatomical study was undertaken to determine the relationship between expelled human placenta of normotensive and hypertensive mothers from term pregnancies and to view the reflections it provides regarding its effect on the growth and wellbeing of the foetus.

Since all anabolites needed for foetal metabolism come from mother's blood and foetal catabolites are passed back into the mother's circulation through 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 future.

Hypertensive disorders of pregnancy, particularly eclampsia (convulsions), result in about 13% of all maternal deaths. They can be prevented through careful monitoring during pregnancy [20, 21].

Hypertension is one of the common medical complications of pregnancy and contributes significantly to maternal deaths and perinatal morbidity and mortality. Hypertension is a sign of underlying pathology which maybe pre-existing or appears for the first time during pregnancy. In developing countries with inadequately cared pregnancy this entity on many occasions remains undetected till major complications supervene.

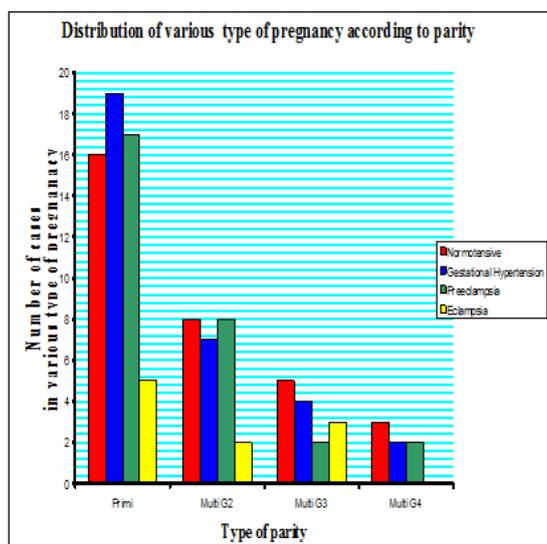
**Table-1: Showing distribution of various types of pregnancy in different parity**

Parity	Normotensive	Gestational Hypertension	Preeclampsia	Eclampsia
Primi	16	19	17	5
Multi G <sub>2</sub>	8	7	8	2
Multi G <sub>3</sub>	5	4	2	3
Multi G <sub>4</sub>	3	2	2	0
<b>Sum</b>	<b>32</b>	<b>32</b>	<b>29</b>	<b>10</b>
<b>Mean</b>	<b>8.000</b>	<b>8.000</b>	<b>7.250</b>	<b>2.500</b>
<b>S.D.</b>	<b>±5.715</b>	<b>±7.616</b>	<b>±7.089</b>	<b>±2.082</b>
<b>S.E.M.</b>	<b>±2.852</b>	<b>±3.807</b>	<b>±3.544</b>	<b>±1.040</b>

In Table-1 we have seen the total number of cases in normotensive, gestational hypertension, preeclampsia and eclampsia according to parity. The mean number of cases in normotensive pregnancy is 8 with a Standard Deviation of ±5.715 and Standard Error of Mean ±2.852. On the other hand in gestational hypertension the mean number of cases is 8, Standard Deviation is ±7.616 and Standard Error of Mean is ±3.807; that of preeclampsia is 7.250, ±7.089 and ±3.544 and that of eclampsia is 2.500, ± 2.082 and ± 1.040 respectively which is evident in fig. no.1

these cases, 16 are primigravida, 8 are multigravida (G<sub>2</sub>), 5 are G<sub>3</sub> and 3 are G<sub>4</sub>. The total number of cases with gestational hypertension are 32, out of which 19 are primigravida, 7 are multigravida (G<sub>2</sub>), 4 are G<sub>3</sub> and 2 are G<sub>4</sub>. The total number of cases with preeclampsia are 29, out of which, 17 are primigravida, 8 are multigravida (G<sub>2</sub>), 2 are G<sub>3</sub> and 2 are G<sub>4</sub>. The total number of cases with eclampsia are 10, out of which 5 are primigravida, 2 are multigravida (G<sub>2</sub>) and 3 are G<sub>3</sub>. No eclamptic are seen fourth gravida. It is also seen that out of 103 cases selected for the study, 57 cases belonged to 1<sup>st</sup> pregnancy.

From the table it is observed total numbers of 32 normotensive cases are taken for the study. Out of



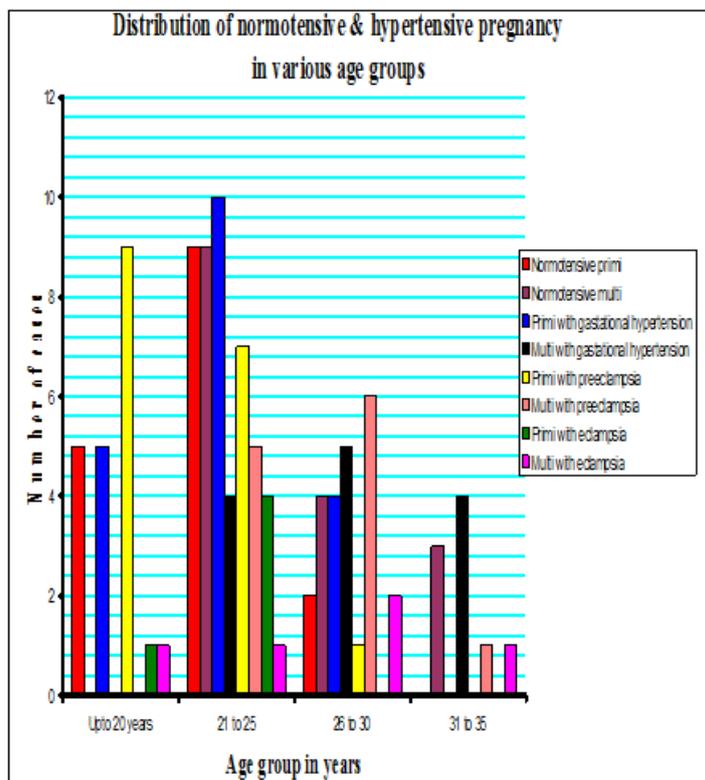
**Fig-1: Showing distribution of various type of pregnancy according to parity**

**Table-2: Showing distribution of normotensive & hypertensive pregnancy in various age groups.**

Age in years	Normotensive		Gestational hypertension		Preeclampsia		Eclampsia	
	Primi	Multi	Primi	Multi	Primi	Multi	Primi	Multi
18 to 20	5	0	5	0	9	0	1	1
21 to 25	9	9	10	4	7	5	4	1
26 to 30	2	4	4	5	1	6	0	2
31 to 35	0	3	0	4	0	1	0	1
<b>Sum</b>	<b>16</b>	<b>16</b>	<b>19</b>	<b>13</b>	<b>17</b>	<b>12</b>	<b>5</b>	<b>5</b>
<b>Mean</b>	<b>4.000</b>	<b>4.000</b>	<b>4.750</b>	<b>3.250</b>	<b>4.250</b>	<b>3.000</b>	<b>1.250</b>	<b>1.250</b>
<b>S.D.</b>	<b>±3.916</b>	<b>±3.742</b>	<b>±4.113</b>	<b>±2.217</b>	<b>±4.425</b>	<b>±2.944</b>	<b>±1.893</b>	<b>±0.500</b>
<b>S.E.M.</b>	<b>±1.957</b>	<b>±1.870</b>	<b>±2.056</b>	<b>±1.108</b>	<b>±2.212</b>	<b>±1.471</b>	<b>±0.946</b>	<b>±0.250</b>

In the above table it is seen that in both normotensive primigravida and multigravida the mean is 4.000 but the Standard Deviation and Standard Error of Mean for primigravida are  $\pm 3.916$  and  $\pm 1.957$  that of multigravida are  $\pm 3.742$  and  $\pm 1.870$  respectively. On the other hand the mean , Standard Deviation and Standard Error of Mean for gestational hypertension in

primigravida are 4.750 ,  $\pm 4.113$  and  $\pm 2.056$  and in multigravida are 3.250 ,  $\pm 2.217$  and  $\pm 1.108$  ; that of preeclamptic primigravida are 4.250 ,  $\pm 4.425$  and  $\pm 2.212$  ; preeclamptic multigravida are 3.000 ,  $\pm 2.944$  and  $\pm 1.471$ ; eclamptic primigravida are 1.250 ,  $\pm 1.893$  and  $\pm 0.946$  and eclamptic multigravida are 1.250 ,  $\pm 0.500$  and  $\pm 0.250$  respectively.



**Fig-2: Showing distribution of age groups in different types of pregnancy**

**Table-3: Showing percentage of different type of histological findings according to the type of pregnancy**

Histological findings	Type of pregnancy			
	Normotensive	Gestational hypertension	Preeclampsia	Eclampsia
Mature villi	90.62 (29)	68.70 (22)	41.37 (12)	20.00 (2)
Hypermature Villi	3.12 (1)	56.25 (18)	68.96 (20)	70.00 (7)
Stromal fibrosis	6.24 (2)	50.00 (16)	62.06 (18)	80.00 (8)
Increased syncytial knot	12.50 (4)	75.00 (24)	72.41 (21)	90.00 (9)
Decidual haematoma	9.37 (3)	46.87 (15)	62.06 (18)	60.00 (6)
Endarteritis	3.12 (1)	37.70 (12)	68.96 (20)	60.00 (6)
Fibrin deposition	12.50 (4)	31.25 (10)	75.86 (22)	70.00 (7)
<b>Sum</b>	<b>137.47</b>	<b>365.77</b>	<b>451.68</b>	<b>450.00</b>
<b>Mean</b>	<b>19.639</b>	<b>52.253</b>	<b>64.526</b>	<b>64.286</b>
<b>S.D.</b>	<b><math>\pm 31.546</math></b>	<b><math>\pm 15.763</math></b>	<b><math>\pm 11.389</math></b>	<b><math>\pm 22.254</math></b>
<b>S.E.M.</b>	<b><math>\pm 11.923</math></b>	<b><math>\pm 5.957</math></b>	<b><math>\pm 4.307</math></b>	<b><math>\pm 8.410</math></b>

N.B- The bracketed figure indicates the number of placenta in which histological findings have been observed

In the above table it is observed that mature villi is seen to be highest in normotensive group (90.6%) and mature villi is gradually decreasing with severity of PIH whereas hypermature villi (70%), stromal fibrosis (80%) and syncytial knot (90%) were

found to be highest in the placenta of eclamptic cases and decidual hematoma ( 62.06%), endarteritis ( 68.96%) and fibrin deposition (75.86%) were found to be maximum in placenta of preeclamptic cases which is evident in figure no. 11.

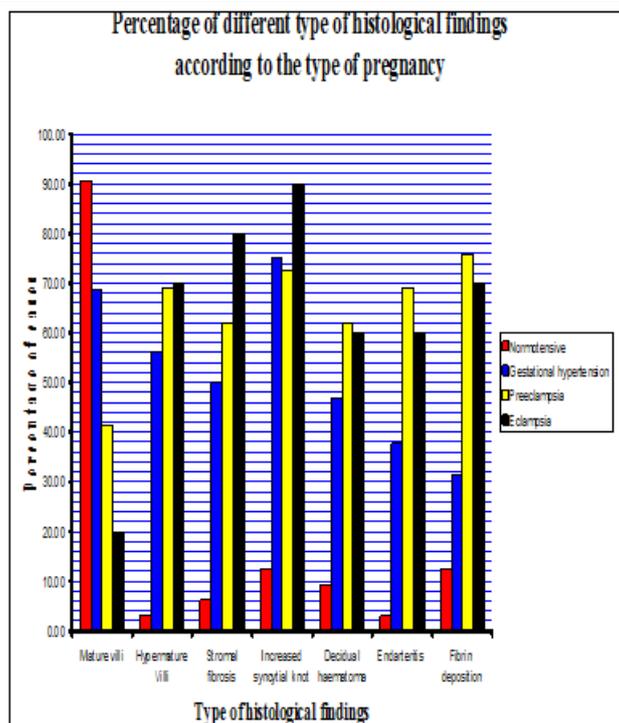


Fig-3: Showing percentage of different type of histological findings

### SUMMARY

1. A careful and detailed study of 103 placentae was done to see the effects of Pregnancy Induced Hypertension on placentae (microscopic) and its relation to birth weight of baby.
2. For the study 32 placentae were collected from normotensive pregnancies and 71 from different groups of hypertensive pregnancies from the Obstetrics and Gynaecology department of Guwahati Medical College, Guwahati (gestational hypertension-32 cases, preeclampsia-32 cases, eclampsia-10 cases).
3. All the cases under study were free from medical as well as obstetrical problems, except for the hypertensive group which revealed only Pregnancy Induced Hypertension.
4. All the cases were of age between 18 to 35 years who had undergone spontaneous vaginal delivery at term and the process of delivery was uneventful.
5. The parity of the patients from where the placentae were collected varied from primigravida to fourth gravida. Majority of the placenta were collected from primigravida mothers i.e. 55.33%.
6. The placentae were preserved in 10% formol saline for 7 days and tissue bits were taken for processing and staining with Haematoxylin and Eosin.
7. In placenta of control group predominance of mature villi is seen (90.62%) whereas frequency of hypermature villi is seen in the placenta of eclamptic mothers (70%). In normotensive placenta only 3.12% show hypermature villi.
8. Incidence of stromal fibrosis is not very significant in normotensive pregnancy (6.24%) whereas high rate of fibrosis is seen in eclampsia (80%),

9. Increased syncytial knot formation was seen towards eclamptic state (90%). In normotensive cases only 12.50% placenta show increased syncytial knot formation.
10. Decidual haematoma as compared to normal is found to be increased in eclampsia (60%), preeclampsia (62.06%) and gestational hypertension (46.8%).
11. Incidence of obliterative endarteritis is found to increase in preeclampsia i.e. 69.96% and eclampsia (60%) but in gestational hypertension and normotensive pregnancy the incidence is not significant.
12. Deposition of fibrin is observed as a common phenomenon in each category of placenta. But the rate of fibrin deposits is highest in preeclampsia (76.86%) and eclampsia (70%) and lowest in normotensive pregnancy (12.50%).
13. Comparison of histological findings in the placenta of normotensive mothers with that of hypertensive mothers shows a statistically highly significant difference with  $p < 0.001$ .
14. The average baby weight in normotensive primigravida is 3.95 kg and that in multigravida is 2.91 kg; in primigravida with gestational hypertension is 2.91 kg and multigravida is 2.83 kg; in preeclamptic primigravida is 2.42 kg and multigravida is 2.41 kg and that in eclampsia is 2.02 kg and 1.66 kg respectively.
15. The mean baby weight in primigravida is higher than the mean baby weight of multigravida irrespective of grades of hypertension.

16. Comparison of baby weight of normotensive mothers with that of hypertensive mothers did not show significant statistical difference i.e.  $p > 0.05$  even though there was reduced birth weight with increasing severity of hypertension.
17. Though no definite correlation between placental changes and foetal outcome is found in this study both placental and foetal weight tended to decrease in pregnancy induced hypertension in comparison to normotensive pregnancy.

### CONCLUSION

The effects of maternal hypertension on the placenta have been studied with emphasis on some important histological parameters:

1. Histological findings like hypermature villi, stromal fibrosis and syncytial knots are seen in higher range in eclampsia whereas decidual haematoma, obliterative endarteritis and fibrin deposition are more in preeclampsia cases.
2. The average birth weight of baby is comparatively lower in hypertensive group but difference in weight in both control and study group is not statistically significant i.e.  $p > 0.05$ .
3. The relationship between both groups would have been more conclusive if more cases would have been available for study with detailed clinical correlation.

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