

# HISTOPATHOLOGICAL STUDY OF FULL-TERM PLACENTA IN SELECTED NORMOTENSIVE AND PRE-ECLAMPTIC WOMEN IN BANGLADESH

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## **Abstract:**

*Pre-eclampsia is a disorder of 2nd half of pregnancy, which is characterized by a combination of hypertension, proteinuria and edema, secondary to decreased placental perfusion. Clinical studies suggest that there are histopathological changes in the placenta of pre-eclamptic women, compared to normotensive pregnant women. In developing countries, pre-eclampsia causes an estimated 50,000 maternal deaths per year. Only a small number of studies have however, been conducted in Bangladesh.*

**Objective:** *To compare the histopathology of placenta in selected pre-eclamptic and normotensive pregnant women.*

**Methods:** *220 pregnant women were selected with inclusion and exclusion criteria from 3 different medical colleges and divided into 2 groups – A study group, consisting of 110 pre-eclamptic women and a control group consisting of 110 normotensive pregnant women. Dietary information was collected by 7 days food frequency questionnaire and food score was determined. Anthropometric and biochemical tests were performed. To evaluate the histopathology of placenta, tissue samples were collected from the placenta after delivery, and were prepared for histopathological studies, by haematoxylin and eosin stain method. The mean number of areas of syncytial knot formation, the mean number of areas of cytotrophoblastic cell proliferation, the mean number of areas of fibrinoid necrosis, and the mean number of areas of hyalinised villi of pre-eclamptic and normal pregnant women were evaluated.*

**Results:** *The mean number of areas of syncytial knot formation, the mean number of areas of cytotrophoblastic cell proliferation, the mean number of areas of fibrinoid necrosis, and the mean number of areas of hyalinised villi were found to be significantly higher in the study group, compared to the control group.*

**Conclusion:** *Therefore, mean number of areas of syncytial knot formation, the mean number of areas of cytotrophoblastic cell proliferation, the mean number of areas of fibrinoid necrosis is increased in the placenta of pre-eclamptic women, compared to normotensive pregnant women.*

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## **Introduction:**

The placenta is a temporary structure unique to pregnancy function to sustain and protect the fetus until birth.<sup>1</sup> It obtains its metabolic, immunological requirements and secretory functions to support fetal developments.<sup>2,3</sup> The placenta is attached to the uterus, and the fetus is connected to the placenta via the umbilical

cord.<sup>4</sup> The human placenta is hemomonochorial, meaning that only one chorionic cell layer exists between maternal and fetal bloods<sup>5</sup> thereby allowing nutrient uptake, waste elimination and gas exchange via the mother's blood supply<sup>6</sup>. The placenta clips to the wall of uterus, usually the top, side, front or back of the uterus and umbilical cord results from it.

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However, in rare cases, placenta might be found in the lower region of the uterus<sup>7</sup>. A term placenta is measures about 2.0 to 2.6 cm thick and 23 cm in diameter. A term placenta usually weighs approximately 470g to 508g with 500 ml of an average volume.<sup>8</sup>

Measurements of placenta differ broadly and substantially in distinct regions<sup>9</sup>. Studies exhibited fetal or maternal illnesses such as acute anaemia, hypertension, and in addition fetal hydrops affect fetal as well as placental weight.<sup>10,11</sup> Race and socioeconomic position affects the placental weight.<sup>12</sup> In Asia report of placental weight is 588g and 470g in Ukraine.<sup>12,13</sup>

The shape of the placenta is extremely variable, probably due to placental location. It is thought to be influenced by its implanted position in the uterus, its interaction with the endometrium and uterine shape.<sup>14</sup> It usually shows an ovoid shape with a 16-20 cm diameter and a 2-3 cm thickness and it grows exponentially during gestation, from an average of 6 gm at 3 week of gestation to 470 gm at term.<sup>15</sup> The placenta implants anywhere in the uterus, but most commonly, it is in an anterior or posterior location, much less often it is on the fundus.<sup>16</sup>

One of the prominent innovations in early mammalian embryogenesis is the formation of the placenta. By 21 days after fertilization the trophoblasts have begun to sort themselves out into what will become the tree-like structures that make up the placenta.<sup>17</sup>

The trophoblast cells are a major component in the placenta<sup>18</sup> and are fetal epithelial cells that form an interface between mother and offspring.<sup>19</sup> In human, the trophoblast cells are tumor-like in their aspect of invasion. However, their invasiveness is precisely controlled in a way that spatially the cells stop penetration at the inner third of the myometrium, and temporarily, the invasion occurs only at the early stage of pregnancy.<sup>20</sup> The human trophoblast differentiates along two pathways<sup>21,22</sup>:

- The Villous trophoblast pathway including the cytotrophoblastic cells differentiates by fusion to form the syncytiotrophoblast that covers the entire surface of the villi.
- The extravillous trophoblast pathway.

The finger-like chorionic villi are the main functional units of the placenta<sup>17</sup> mediating nutrient absorption, waste elimination and generating the bulk of the hormones produced by the placenta during pregnancy.<sup>3</sup>

### Materials and Method

A comparative cross sectional study was done for three years from June 2015 to May 2018. Study groups were selected from three major tertiary hospitals located in Dhaka City: Dhaka Medical College and Hospital, Sir Salimullah Medical College and Mitford Hospital and Holy Family Red Crescent Medical College and Hospital. To calculate the prevalence and proportion of pre-eclampsia, we followed the standard procedure. A total number of 10,800 pregnant patients, admitted in Gynae and Obs Department of aforesaid hospitals from June, 2015 to May, 18 were selected. Amongst them, a total of 1800 were complicated with pre-eclampsia. So, Sample size was calculated, n=217. Selection of cases was based on strict inclusion and exclusion criteria: Incase of pre-eclamptic women age groups: 18 to 40 years, Pregnancy status: third trimester of pregnancy, Blood Pressure: Diastolic Blood Pressure above 90 mm of Hg. Clinically oedema of legs present; Proteinuria: Confirmed by biochemical tests. Exclusion Criteria: Less than 18, greater than 40; No oedema; No proteinuria; Normal Blood Pressure (diastolic <90 mm of Hg). A questionnaire was developed to obtain relevant information regarding socio economic status, age, obstetric history, monthly income, living area, family size, education, type of jobs and usual habit of food before admission to hospital. Ethical permission has been obtained from Ethical review committee of Bangladesh Medical and Research Council (B.M.R.C). Written consent was taken from both pre-eclamptic and normal pregnant women. To evaluate the histopathology of placenta, tissue samples were collected from the placenta after delivery, and were prepared for histopathological studies, by haemotoxylin and eosin stain method. The mean number of areas of syncytial knot formation, the mean number of areas of cytotrophoblastic cell proliferation, the mean number of areas of fibrinoid necrosis, and the mean number of areas of hyalinised villi of pre-eclamptic and normal pregnant women were evaluated. Haematological and BioChemical Assays: CBC, HB%, ESR and Fasting Blood

Sugar, serum Vit C and serum Vit E, Urine for Albumin: assessed by Heat Coagulation Test were measured. Nutritional Status: measured by Mid Upper Arm Circumference (MUAC), using a measuring tape (in cm). Dietary Information: Dietary information was measured by 7 days food frequency questionnaire. Measurement of weight: Body weight was measured by bathroom scale, to the nearest 0.5 kg. Measurement of height: A wooden height scale was used to

record height with bared heels, standing in upright position, height was measured to nearest 0.1 cm. Blood Pressure Measurement: The blood pressure was measured by sphygmomanometer machine and stethoscope. Birth weights of new born babies: Birth weights of new born babies were recorded to the nearest 20 grams after delivery without clothes on a beam balance (Dedecto medic, Delecto scale inc., U.S.A.)

## Results:

**Table-I**  
*Distribution of respondents according to Hospital*

Hospitals	Pre-eclamptic Women (Study Group A) N=110		Normal Pregnancy (Control Group - B) N = 110	
DMCH	70	63.64%	70	63.64%
Mitford	30	27.27%	30	27.27%
HFRCMH	10	9.09%	10	9.09%
Total	110	100%	110	100%

Table I: shows 63% respondents were from DMCH, 27% from Mitford, and 9% from HFRCH

**Table-II**  
*Anthropometric and clinical indices*

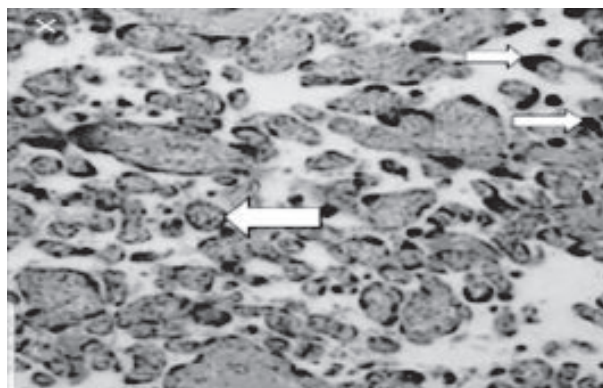
N=220	Pre - Eclamptic (Group - A) n= 110 (Mean ± STD.)	Normal Pregnant Women (Control - B) n = 110 (Mean ± STD.)	P. Value
Weight (Kg.) of the Patient	66.65±5.34	66.9±2.05	0.65
Height (cm.) of the Patient	154.06±3.58	156.003±3.36	0.62
MUAC (CM)	23.5±2.64	25.1.1±2.24	0.001
Systolic Blood Pressure (mm/Hg)	125.14±28.34	117.27±4.47	0.001
Diastolic Blood Pressure (mm/Hg)	98±5.55	79±3.51	0.001
Wt. of Babies (Kg.)	2.09 ± 0.13	2.80 ± 0.12	0.001

Table II, shows mean MUAC, systolic and diastolic BP, weight of new born Babies of Study and Control Group were different, it was statistically, significant.

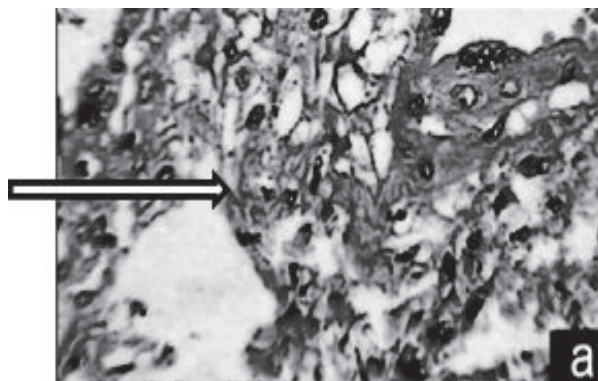
**Table-III**  
*Mean No. Areas of Syncytial Knot Formation in pre-eclamptic and normal pregnant women*

Mean No. Areas of Syncytia	Pre-eclamptic Women (Group-A) N=110 (Mean ±SD)	Normal Pregnant Women Control Group - B N=110 (Mean ±SD)	P. Value
1 Knot Formation	26.76 ± 3.86	9.60 ± 1.46	0.001

Table III shows that mean no. areas of syncytial knot formation of pre-eclamptic women (26.76 ± 3.86) was significantly (p-value .001) higher than the mean no. areas of syncytial knot formation of normal pregnant women (9.60 ± 1.46).



Syncytial knot formation



Cytotrophoblastic cell proliferation

Table IV shows that mean no. of areas of cytotrophoblastic cell proliferation of pre-eclamptic women ( $21.52 \pm 5.03$ ) was significantly ( $p$ -value .001) higher than the mean no. of areas of cytotrophoblastic cell proliferation of normal pregnancy women ( $7.16 \pm 2.06$ ).

Table 5 shows that mean no. of areas of fibrinoid necrosis of pre-eclamptic women ( $10.68 \pm 3.33$ ) is significantly ( $p$ -value .001) higher than the mean no. of areas of fibrinoid necrosis of normal pregnancy women ( $2.24 \pm 0.69$ ).

**Table IV**

*Mean No. Areas of Cytotrophoblastic Cell Proliferation in pre-eclamptic and normal pregnant women.*

Mean No. of Areas of Cytotrophoblastic Cell Proliferation	Pre-eclamptic Women (Group-A) N=110 (Mean $\pm$ SD)	Normal Pregnant Women Control Group - B N=110 (Mean $\pm$ SD)	P. Value
	$21.52 \pm 5.03$	$7.16 \pm 2.06$	0.001

**Table-V**

*Mean No. of Area of Fibrinoid Necrosis in pre-eclamptic and normal pregnant women*

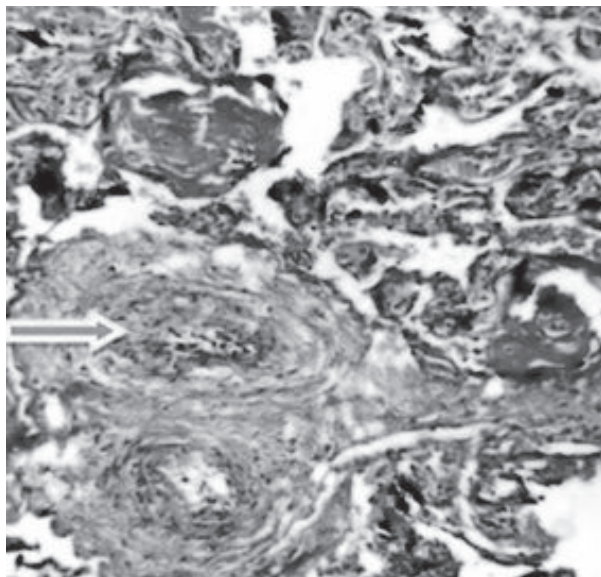
Mean No. of Area of Fibrinoid Necrosis	Pre-eclamptic Women (Group A) N=110 (Mean $\pm$ SD)	Normal Pregnant Women Control Group - B N=110 (Mean $\pm$ SD)	P. Value
	$10.68 \pm 3.33$	$2.24 \pm 0.69$	0.001

**Table-VI**

*Mean number of Areas of Hyalinised Villi. Of Pre-eclamptic and normal pregnant women*

Mean No. of Area of Hyalinised Villi	Pre-eclamptic Women (Group-A) N=110 (Mean $\pm$ SD)	Normal Pregnant Women Control Group - B N=110 (Mean $\pm$ SD)	P. Value
	$9.46 \pm 4.10$	$2.32 \pm 0.59$	0.001

Table 6 shows that mean no. of areas of hyalinised villi of pre-eclamptic women ( $9.46 \pm 4.10$ ) was significantly ( $p$ -value .001) higher than the mean no. of areas of hyalinised villi of normal pregnancy women ( $2.32 \pm 0.59$ ).



*Fibrinoid Necrosis*

#### **Discussion:**

The present study was conducted amongst 220 pregnant women to see the effect of pre-eclampsia on the histology of placenta. So far, few studies like this have been conducted in Bangladesh.

In his studies, Cibils<sup>24</sup> found that in hypertensive patients, the overall size of the placentas were considerably reduced, which indicated that the growth process was interrupted by high blood pressure, whereas in another study, Shah et al<sup>23</sup> noticed that with increasing severity of pre-eclampsia, the weight of placenta was further reduced.

According to Fox<sup>25</sup>, Jones<sup>26</sup> and Soma et al<sup>27</sup>, the histomorphological abnormalities in hypertensive placenta are due to occlusion or narrowing of the uteroplacental vessels as well as placental ischemia. In pre-eclampsia the balance between formation of free radicals, and antioxidant mediated defense is disrupted, leading to abnormalities of endothelial function and free radical-mediated endothelial cell injury.<sup>28,29</sup>

Placental infarction was more in case of pre-eclamptic women compared to normal normotensive pregnant women<sup>30</sup>. It was also observed by Mirchandani *et al*<sup>31</sup> and Masodkar *et al*<sup>32</sup>.

Segupta kishwara et al., (2010); and several others (Abu Sadat Mohammad Nurunnabi, Mahamuda Begum, Abu Rayhan, Shamim Ara)<sup>33</sup> observed that the mean diameter of placenta, ( $16.08 \pm 2.08$  cm), mean number of cotyledons were ( $14.30 \pm 2.47$ ) was less in the study group, compared to the control group ( $18.80 \pm 2.32$ cm) and ( $15.77 \pm 2.80$ ) respectively. They also observed increased number of infarcted areas, 15, in the placenta of study group, compared to the control group, which were only 4.

This study also reveals that mean number of areas of syncytial knot formation (26.76), cytotrophoblastic cell proliferation (21.52), area of fibrinoid necrosis(10.68), and hyalinised villi (9.46) were increased in case of pre-eclamptic women, compared to normal pregnancy which were (9.60), (7.16) (2.24) and (2.32) respectively.<sup>33</sup> M. Akhlag., 2012; and others (AH Nage, AW Yousuf) also observed increased syncytial knot formation ( $25.23 \pm 1.23$ ) in pre-eclamptic women compared to normal pregnant women. Other studies have also found similar results, with increased syncytial knots formation ( $26.31 \pm 2.72$ ); cytotrophoblastic cell proliferation ( $22.53 \pm 1.74$ ) fibrinoid necrosis ( $9 \pm 2.96$ ) and hyalinized villi ( $8.96 \pm 2.42$ ), in pre-eclamptic patient.

K Devi Shankar and others observed that there is a reduced placental weight, placental thickness, placental diameter and neonatal weight in pre-eclamptic women compared to normal pregnant women<sup>34</sup>. In another study, it showed that there is an increase in syncytial knot formation in pre-eclamptic women compared to normal pregnant women<sup>35,36,37</sup>. In another study they found increased fibrinoid necrosis in pre-eclamptic women compared to normal pregnant women.<sup>38,39,30,32</sup>

#### **Conclusion:**

This was a comparative study to evaluate the histological changes of placenta in pre-eclamptic

women . Our study revealed that the mean number of areas of syncytial knot formation, the mean number of areas of cytotrophoblastic cell proliferation, the mean number of areas of fibrinoid necrosis, and the mean number of areas of hyalinised villi were significantly higher in the study group, compared to the control group.

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