

## A study on histopathological changes in placenta in pre-eclampsia/eclampsia: A case-control study in tertiary care centre, western India

CR Gore<sup>1</sup>, Aditi Pandey<sup>2,\*</sup>, Abhinav Shetty<sup>3</sup>, Ruby Rao<sup>4</sup>, Sourabh Paranjape<sup>5</sup>

<sup>1</sup>Professor, <sup>2,3,4,5</sup>Resident Dept. of Pathology, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D.Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, India

\*Corresponding Author:

Email: draditipandey@gmail.com

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### Abstract

**Introduction:** In pregnancy induced hypertension (PIH), pathological changes in the placenta occurs which may result in reduced blood flow across placenta. The present study has been undertaken to assess the morphology & histology of placenta from mothers with PIH and to correlate their findings with those of normal pregnancies.

**Materials and Methods:** The present study was a case-control study conducted during July 2015 to September 2017. Placenta of cases of singleton normal pregnancies & those complicated by pre-eclampsia/ eclampsia and of known gestational period were included. The placentae were divided into two groups; Group 1: Pregnancy with hypertension (cases) and Group 2: Normal pregnancy (control). Detailed macroscopic and microscopic examinations were conducted on the placentae.

**Results:** The mean weight of placenta ( $474 \pm 58$  grams) was higher among control group in comparison to PIH group ( $420 \pm 61$  grams). This difference was statistically significant. ( $p < 0.001$ ) The mean fetoplacental weight ratio ( $6.14 \pm 0.503$ ) was higher among PIH group in comparison to control group ( $6.03 \pm 0.409$ ). This difference was statistically insignificant. ( $p < 0.05$ ). There was significant association between presence of gross infarction, calcification, Hyalinised area /10 lpf, medial coat proliferation/ 10 lpf, intervillous hemorrhage, decreased villous vascularity and PIH.

**Conclusion:** It is concluded that there was statistically significant difference between mean birth weight of the babies and mean placental weight in control group and PIH group. It also revealed striking villous lesions like increased syncytial knots, cytotrophoblastic cell proliferation, villous stromal fibrosis and fibrinoid necrosis in placenta from preeclampsia cases.

**Keywords:** Placenta, Histopathological Changes, Pre-eclampsia, Eclampsia.

### Introduction

Hypertensive disorders complicating pregnancy are common. It forms one of the deadly triad, along with haemorrhage & infection, which contribute greatly to maternal & foetal morbidity & mortality.<sup>1</sup>

In pregnancy induced hypertension (PIH), pathological changes in the placenta such as infarction, calcifications, diffuse placental thrombosis, inflammatory placental vasculopathy and abnormal trophoblastic proliferation occur. It results in reduced blood flow across placenta and uteroplacental insufficiency.<sup>2</sup>

Naeye and Friedman (1979) calculated that 70% of excess foetal deaths in women with hypertension are due to placental infarcts. It has been recorded that the maternal utero-placental blood flow is decreased in PIH due to maternal vasospasm. It causes indirect constriction of foetal stem arteries. Babies of such mothers are mostly small for date.<sup>3</sup>

Histological findings like cytotrophoblastic cellular proliferation, syncytial knot formation, fibrin plaque formation etc. have been observed in greater amount in hypertensive placentae.<sup>4,5</sup>

Gross pathological changes are commonly seen in placentae of severe preeclampsia. The characteristic placental changes of preeclampsia would be predicted to be those associated with placental ischemia. In consistence with this prediction, the placenta in

preeclampsia is small. The gross placental changes with severe preeclampsia and foetal growth retardation are quite similar.<sup>6,7</sup>

In view of this, the study of placenta should provide insight into the pathophysiology of pre-eclampsia. The present study has been undertaken to assess the morphology & histology of placenta from mothers with pre-eclampsia/eclampsia and to correlate their findings with those of normal pregnancies.

### Materials and Methods

The present study was a case-control study conducted in the Department of Pathology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune in close association with the Department of Obstetrics and Gynecology at our hospital during July 2015 to September 2017.

Placentae of cases of singleton normal pregnancies & those complicated by pre-eclampsia/ eclampsia were included in the study. The placentae of pregnancies complicated by other medical disorders like diabetes mellitus etc., multiple pregnancies and preterm pregnancies were excluded.

The placenta received from the Department of Obstetrics and Gynecology was divided into two groups.

**Group 1: Pregnancy with Hypertension (cases):** Placenta of patients (with B.P. > 140/90 mmHg after 28

weeks of gestation, with/without edema, and/or proteinuria, and/or convulsion)

**Group 2: Normal Pregnancy (control):** Placenta of uncomplicated term pregnancies with a gestation between 28wks and 40wks with no foetal or maternal complications.

Clinical details of mothers like general condition, pallor, BP, edema, history of previous child birth, past illness were recorded on predesigned questionnaire. The routine investigations were also noted. Weight of the placenta and neonate was noted.

For macroscopic examination, placenta were washed, blood and blood clots were removed. Perfusion of placenta with 10% formalin through umbilical vessels was followed by immersing the placenta in a jar containing 10% formalin for 24 hours.

After 24hrs of fixation in formalin, gross examination of the placentae for presence of any infarction, calcification and retro placental clots was done.

For microscopic examination, sections were stained with haematoxylin and eosin stain. Slides were studied under the compound microscope for study of Placental villi, size of villi, syncytial knot formation, hyalinization, fibrinoid necrosis, cytotrophoblastic proliferation, Stromal pathology, stromal fibrosis, calcification, hyalinization and intervillous hemorrhage.

## Result

The present study included 30 placentae of women with PIH and 30 of normal pregnancy. The mean maternal age of control group was  $23.5 \pm 3.85$  years and that of PIH category was  $24.8 \pm 2.67$  years. The mean gestational age of control group was  $39.13 \pm 1.95$  weeks and that of PIH category was  $38.8 \pm 1.12$  weeks. There was no significant association between maternal age, gestational age among control and PIH group (Table 1). (p value >0.05)

**Table 1: Maternal age group and gestational age wise distribution of study subjects**

Age group	Control (n=30)		PIH (n=30)		Total (n=60)	
	No.	%	No.	%	No.	%
20 and below	8	26.7	2	6.7	10	16.7
21-25	15	50	16	53.3	31	51.7
26-30	5	16.6	11	36.7	16	26.6
31-35	2	6.7	1	3.3	3	5.0
<b>Total</b>	30	100	30	100	60	100
Gestational age (weeks)	Control (n=30)		PIH (n=30)		Total (n=60)	
	No.	%	No.	%	No.	%
37	2	6.7	4	13.3	6	10
38	9	30	8	26.7	17	28.3
39	6	20	10	33.3	16	26.7
40	9	30	6	20.0	15	25
41	4	13.3	2	6.7	6	10
<b>Total</b>	30	100	30	100	60	100

**Table 2: Mean of birth weight, placental weight and feto-placental weight ratio**

	Control (n=30)	PIH (n=30)	P value
Mean birth weight (gms)	2853	2516	0.003
Mean placental weight (gms)	474	420	0.001
Mean fetoplacental weight ratio	6.03	6.14	0.47

The mean of birth weight, placental weight and fetoplacental ratio was as shown in Table 2. In control group, mean birth weight of babies was higher ( $2853 \pm 320$ gms) in comparison to PIH group ( $2516 \pm 385$ gms). This difference was found statistically significant. (p value 0.003). The mean weight of placenta ( $474 \pm 58$  grams) was higher among control group in comparison to PIH group ( $420 \pm 61$  grams).

This difference was statistically significant. (p 0.001) The mean fetoplacental weight ratio ( $6.14 \pm 0.503$ ) was higher among PIH group in comparison to control group ( $6.03 \pm 0.409$ ). This difference was statistically insignificant. (p >0.05)

**Table 3: Placental morphology in study group**

Placental Morphology	Control (n=30)		PIH (n=30)		P value
	No.	%	No.	%	
Infarction (gross)	1	3.3	20	66.7	0.001
Calcification (gross)	11	36.7	26	86.7	0.001
Hyalinised area /10 lpf	3	10.0	15	50.0	0.003
Medial coat proliferation/ 10 lpf	2	6.7	23	76.7	0.001
Intervillous hemorrhage	3	10.0	22	73.3	0.003
Decreased Villous Vascularity	0	0	22	73.3	0.001

On analyzing gross and microscopic features of the placentae, there was significant association between presence of gross infarction, calcification among control group and cases. Microscopic features also showed significant differences. (Table 3) Comparison

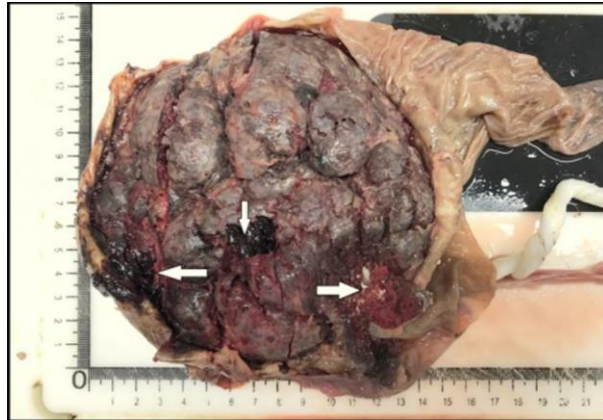
of microscopic features of placenta among the PIH and control group were as shown in Table 4. Comparison of placental morphology among study participants was as shown in table 5.

**Table 4: Distribution of study subjects according to microscopic features of placenta**

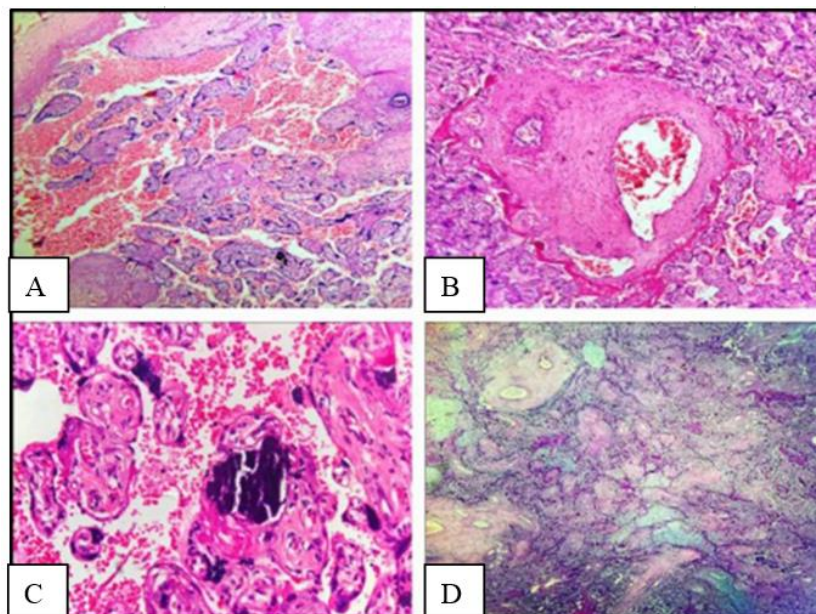
Microscopic features	Control (n=30)		PIH (n=30)	
	No.	%	No.	%
<b>No. of Syncytial Knots formation per 100 villi</b>				
0-30	18	60	0	0
31-60	12	40	9	30
61-90	0	0	18	60
91-120	0	0	03	10
<b>No. of areas of fibrinoid necrosis / 100 villi</b>				
01-05	27	90	0	0
06-10	3	10	14	46.7
11-15	0	0	8	26.7
16-20	0	0	7	23.3
21-25	0	0	1	3.3
<b>No. of areas of cytotrophoblastic proliferation</b>				
01-05	23	76.7	0	0
06-10	7	23.3	4	13.3
11-15	0	0	10	33.3
16-20	0	0	11	36.7
21-25	0	0	5	16.7
<b>No. of calcified areas/10 lpf</b>				
0	19	63.3	3	10
1	9	30	4	13.3
2	2	6.7	13	43.4
3	0	0	5	16.7
4	0	0	4	13.3
5	0	0	1	3.3

**Table 5: Comparison of placental morphology among study participants (n=60)**

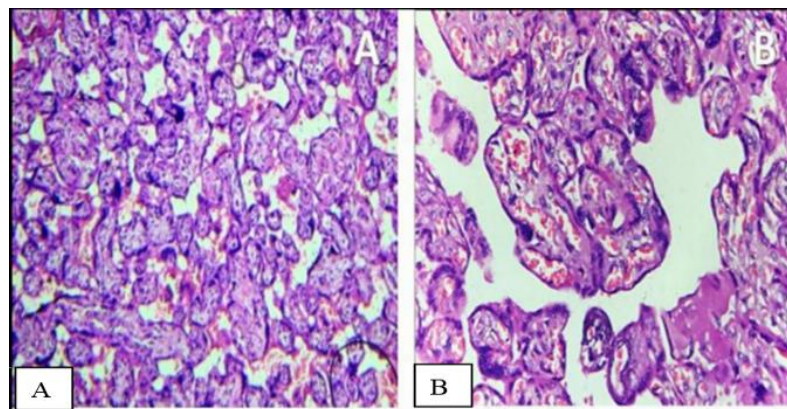
Placental morphology	Group	n	Mean	Std. deviation	P value
Syncytial knots /100 villi	Control	30	29.3	7.84395	0.001
	PIH	30	72.6333	14.8359	
Fibrinoid necrosis /100 villi	Control	30	3.4333	1.56873	0.001
	PIH	30	12.3333	4.39697	
Hyalinized villi / 10 lpf	Control	30	1	0.94686	0.0003
	PIH	30	6.9333	2.50425	
Cytotrophoblastic Proliferation / 100 villi	Control	30	3.6667	2.57753	0.001
	PIH	30	16.2	4.27019	
Calcified areas / 10 lpf	Control	30	0.43	0.626	0.001
	PIH	30	2.2	1.242	



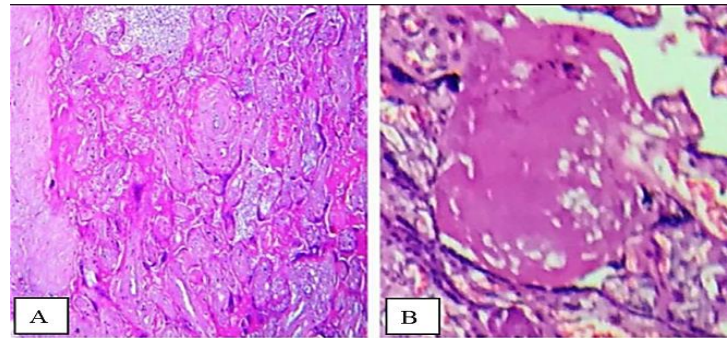
**Fig. 1:** Gross picture of PIH placenta showing haemorrhage and necrosis (white arrows)



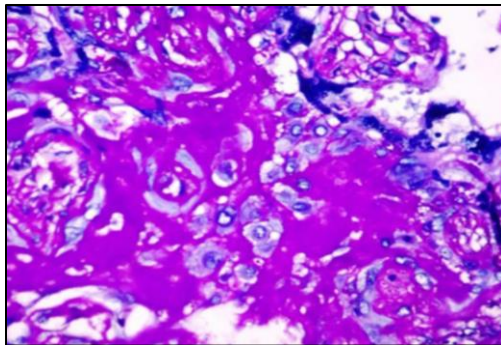
**Fig. 2:** Photomicrograph showing; A). Intervillous haemorrhage (H & E, 100X); B). Vascular medial coat proliferation (H & E, 100X); C). Calcification (H & E, 400X); D). Areas of infarction (H & E, 100X).



**Fig. 3:** Photomicrograph showing; A). Decreased villous vascularity in PIH (H & E, 100X); B). Syncytial knots in pre-eclamptic placenta (H & E, 400X)



**Fig. 4: Photomicrograph showing; A). Extensive fibrinoid necrosis (arrow) (H & E, 100X); B). Fibrinoid necrosis involving entire villous. (H & E, 400X)**



**Fig. 5: Photomicrograph of intervillous fibrin deposition. (Magenta) (PAS, 400X)**

### Discussion

In the present study, mean birth weight of babies was higher ( $2853 \pm 320$ gms) in control group compared to PIH group ( $2516 \pm 385$ gms). This difference was found statistically significant. (p value 0.003). In the study conducted by Shevade et al,<sup>8</sup> the mean foetal weight was 2.1 kg and 2.8 kg in PIH group and control group respectively. S Kishwara et al,<sup>9</sup> Boyd and Scott<sup>10</sup> (1985), Mayhew et al. (2003)<sup>11</sup> Barton et al. (2001)<sup>12</sup> observed that the mean birth weight of the neonate was significantly lower in the group with preeclampsia than that of control group. Odegard et al. (2000)<sup>13</sup> found that preeclampsia was associated with a 5% reduction in birth weight.

The mean fetoplacental weight ratio ( $6.14 \pm 0.503$ ) was higher among preeclampsia group women in comparison to control group ( $6.03 \pm 0.409$ ). However this, difference was statistically insignificant. Majumdar et al<sup>14</sup> found fetoplacental weight ratio of 6.23:1, Nag U et al<sup>15</sup> found 6.02:1, Deepalaxmi Salmani et al<sup>16</sup> found 6.35:1 in PIH group while Majumdar et al<sup>14</sup> found fetoplacental weight ratio of 5.89:1, Nag U et al<sup>15</sup> found 5.94:1, Deepalaxmi Salmani et al<sup>16</sup> found 5.72:1 in control group.

There was significant difference between presence of infarction in control group and PIH group (p value 0.001). (Fig. 1, 2) These findings were similar with the findings of Wentworth et al,<sup>17</sup> Salvatre et al.<sup>18</sup> Infarction occurs due to thrombotic occlusion of maternal uteroplacental blood vessels and is seen in pregnancies

complicated by PIH. There is worsening of uteroplacental ischemia resulting in high incidence of foetal hypoxia, intrauterine growth retardation and foetal death in PIH as stated by Raghvendra et al.<sup>19</sup>

Mean number of syncytial knots was  $72.6 \pm 14.8$  in PIH group while it was  $29.3 \pm 7.8$  in control group which was found significant (0.001). Fig. 3) It was higher in PIH group compared to control group. Similar results have been observed by Saeed et al,<sup>20</sup> Sharma et al,<sup>21</sup> Pasricha et al,<sup>22</sup> Dhabhai et al<sup>23</sup> and Nafees et al.<sup>24</sup> They found higher number of syncytial knots in preeclamptic placenta as compared to control placenta. Khalid et al,<sup>25</sup> Narasimha et al<sup>26</sup> and Tomas et al<sup>27</sup> have also reported the similar findings.

There was statistically significant association between PIH and presence of hyalinised area. (p value 0.0003). (Fig. 4,5) Various workers like Costa et al,<sup>28</sup> Motwani et al<sup>29</sup> and Salgado et al<sup>30</sup> have previously demonstrated hyalinised villi in preeclamptic placenta.

The mean number of cytotrophoblastic proliferation was  $16.2 \pm 4.27$  in PIH group while it was  $3.6 \pm 2.57$  in control group. Our study showed significantly increased cytotrophoblast proliferation in preeclamptic placenta as compared to control placenta. Jones et al<sup>31</sup> found significant increase in number of cytotrophoblast cells in preeclamptic placenta. Narasimha et al,<sup>26</sup> Arnholdt et al,<sup>32</sup> Motwani et al,<sup>29</sup> Nafees et al,<sup>24</sup> Maqueo et al<sup>33</sup> and also found similar results.

There was statistically significant association between PIH and decreased villous vascularity. (Fig. 3) (p value 0.001). Majumdar Set al,<sup>14</sup> Motwani et al<sup>29</sup> and Narasimha et al<sup>26</sup> reported reduced villous vascularity in preeclamptic placenta as compared to control placenta. Saleh et al<sup>34</sup> observed that villi of preeclamptic placenta showed condensed villous connective tissue core and regression of villous capillaries upto complete disappearance.

### Conclusion

It is concluded from the present study that there was statistically significant difference between mean birth weight of the babies and mean placental weight in control group and PIH group. It also revealed striking villous lesions like increased syncytial knots,

cytotrophoblastic cell proliferation, villous stromal fibrosis and fibrinoid necrosis in placenta from preeclampsia cases as compared to placenta from normal term pregnancy. Thus, it can be concluded that preeclampsia has adverse effect on morphology of placenta and consequently affects the foetal outcome.

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