Histomorphometric Study of Maternal Side of Placenta in Preeclampsia

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Background: Preeclampsia is a syndrome peculiar to pregnancy. It affects 5 – 7% pregnancies throughout the world. Although the cause of preeclampsia is unknown, compelling evidence implicates the placenta and the only known cure is removing the placenta i.e. birth of the baby.

Objectives: To determine the effects of preeclampsia on the morphology of maternal side of placenta.

Materials and Methods: 25 normal placentae and 50 placentae from preeclamptic women were obtained from Lady Aitchison hospital Lahore. The basis of selection and distribution of preeclamptic placentae into groups was based on diastolic blood pressure ranging from 90 – 130 mm Hg. Placental weight and volume was measured. On histological examination, the lumen of spiral arteriole and changes in its tunica intima and media were observed.

Results: The study demonstrated that the weight and volume of placentae progressively decreased with mounting blood pressure. On histological examination significant reduction of luminal diameter of spiral arterioles and increased disruption of basement membrane at multiple sites was a feature (33 and 80% respectively) of preeclamptic placentae in groups C and D with diastolic BP 101 – 115 and 116 – 130 mm Hg respectively. Thrombosis was also present in 29 and 40% placentae in severe preeclamptic groups C and D respectively. However, hypertrophy and fibrinoid necrosis was observed even in milder cases.

Conclusions: from the study we concluded that the increase in diastolic blood pressure adversely affected the maternal side of the placentae.

Key words: Placenta, preeclampsia, diastolic blood pressure, spiral arteriole.

Introduction

For implantation to occur, endometrium transforms itself into dense cellular matrix called Decidua.[1] The decidua basalis is part of deciduas deep to the conceptus and forms the maternal component of placenta. Decidua Basalis contains 80 – 100 spiral endometrial arterioles.

Implantation begins with invasion of uterine epithelium and underlying stroma by trophoblast cells derived from blastocyst. Villous cytotrophoblast cells at the tips of stem (anchoring) villi proliferate to form columns from which individual cells migrate into decidual tissue. These trophoblast cells invade as far as the superficial layers of the myometrium.[2] They destroy the endothelial cells and tunica media of the blood vessels as a priming process. This transforms the spiral arterioles into large bore, tortuous vessels of low resistance like sinusoids.[3,4] This vascular transformation is important to ensure an adequate blood supply to the feto-maternal unit. Failure of this process will lead to clinical pathological condition such as miscarriages, intra – uterine growth retardation (IUGR) or preeclampsia.

Preeclampsia is uniquely a disease of pregnancy that effects 7 – 10% of all pregnancies in USA and 5 – 7% through out the world.[5] It is associated with hypertension and proteinurea. The primary cause of preeclampsia is widespread apoptosis of cytotrophoblast cells.[6-8] Tthe invasion of uterine spiral arterioles by trophoblast is limited to the superficial portions of deciduas and 30 – 50% of these arterioles in placental bed escape trophoblast remodeling.[9,10] The myometrial segments of these arterioles remain intact and undilated and their adrenergic nerve supply remains unaffected.[11,12] The mean luminal diameter of uterine spiral arterioles in women with preeclampsia is less than one third of the diameter of similar vessels from uncomplicated pregnancies.[13] Consequently, there is a reduction in uteroplacental perfusion with placenta becoming ischemic as gestation progresses.[14,15] This results in morphological and histological changes in placenta and fetal hypoxia leading to IUGR which contributes to premature delivery and fetal death.[16]

The study was conducted to observe the effects of preeclampsia on the morphology of maternal side of placenta.

Materials and Methods

Twenty five placentae along with umbilical cord from women with normal pregnancies and 50 placentae with umbilical cords from women with preeclampsia were obtained from operation labour room of Lady Aitchison hospital. All these women were examined clinically in the emergency. Their medical history i.e. history of past illness, previous pregnancies, and treatment history was recorded on a proforma.

Selection of Patients

The blood sugar, blood urea, creatinine, haemoglobin and protein urea were recorded. Cases with a range of diastolic blood pressure between 86 – 130 mm Hg, oedema and

protienuera were allocated the preeclamptic group. Patients on any kind of medications or the ones suffering from any concurrent diseases such as hypertension, diabetes mellitus etc. were excluded from the study.

In normal pregnancy groups, only cases with blood pressure between 70 – 85 mm Hg with out oedema and proteinurea were included.

Division of Patients

Patients were categorized into four groups. Group A (control group) had diastolic B. P ranging from 70 – 85 mm Hg, Group B between 86 – 100 mm Hg, Group C between 101 – 115 mm Hg and Group D had blood pressure ranging from 116 – 130 mm Hg (Table 1).

Table 1: *Grouping of patients categorized according to the range of blood pressure and the percentage of preeclamptic patients.*

Parameters	Groups			
	A	B	C	D
Diastolic Blood Pressure (mm Hg)	70 – 85	86 – 100	101 – 115	116 – 130
Number and percentage of patients	25	11 (22%)	24 (48%)	15 (30%)

Samples Collection and Processings

After delivery, placentae were mopped to remove any clotted blood and then weighed after removing the umbilical cord and membranes. Gross examination of the placentae was performed for the measurement of weight, diameter and thickness. These were washed and fixed in 10% formalin. Each placenta was cut into four quadrants.

A sample of 2 × 2 cm was taken from two randomly selected quadrants. Site of selection was from the centre of the maternal side of each quadrant. Separate tissue was taken from any pathological lesion, if present.

Tissue were processed and stained with Haematoxylin and Eosin and Periodic Acid Schiff (PAS) stains.

Adequacy of Sample

These were studied under light microscope and observations were made from 3 randomly selected fields per slide so a total of 12 fields per slide from the maternal side of placenta were examined for each placenta. At least 1 – 2 spiral arterioles were looked for in every placenta under a magnification of 10X. Only one randomly selected spiral arteriole was examined for changes in tunica intima and tunica media.

Histological Parameters

Endothelial atrophy, hypertrophy, disruption and fibrinoid necrosis was observed. The basement membrane was studied for its integrity. In the tunica media, the presence of hypertrophy of smooth muscles was observed. Fibrinoid necrosis of the blood vessels wall, luminal diameter of spiral arteriole and the presence of thrombosis in the lumen of spiral arteriole were noted.

Statistical Analysis

Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS). ANOVA, Post hoc Scheff and Chi square tests were applied to analyze the data.

Results

Out of a total of 50 preeclamptic placentae 11 (22%) fell into Group B, 24 (48%) in Group C and 15, (30%) in Group D.

The mean weight and volume of placentae was significantly reduced in severe preeclamptic Groups C and D ($P < 0.001$) compared to control group A (Table 2).

Table 2: *Mean Values of Gross Parameters in Control and Preeclemptic Placentae.*

Groups	Diastolic Blood Pressure (mm Hg)	Mean Weight (gms.)	Mean Volume (cm^3)
A (n = 25)	70 – 85	588.3 ± 63.3	705 ± 3.41
B (n = 11)	86 – 100	539.5 ± 23.4	534.7 ± 3.55 ***
C (n = 24)	101 – 115	462.9 ± 54.6 ***	306.1 ± 3.40 ***
D (n = 15)	106 – 130	424. ± 67.2 ***	249 ± 3.62 ***

* $p < .05$ significant
** $p < .01$ considerably significant
*** $p < .001$ highly significant

Microscopic Examination

In control group A, spiral arteriole had a mean luminal diameter of 232.68 ± 48.57µm. In group B, endothelium was disrupted in one out of eleven cases (9.09%) and was enlarged in two (18.1%) cases. The basement membrane was disrupted in one case (9%). In tunica media, hypertrophy of smooth muscles was observed in two cases (18.1%) and fibrinoid necrosis effected part of wall of arteriole in two cases (18.1%). The mean luminal diameter was 223 ± 47.6 µm (Table 3).

In preeclamptic Group C, endothelium was enlarged in five out of twenty four cases (20.8%), was atrophied in three (12.5%) cases, underwent fibrinoid necrosis in eight (33.3%) cases and was disrupted in all twenty four (100%) cases. The basement membrane was found disrupted in all 24

Table 3: *Different Pahologies in the Walls of Spiral Arterioles of Placentae in Study Groups.*

Groups	Diastolic blood Pressure (mm Hg)	Tunica Intima								Tunica Media	Fibrinoid Necrosis of Wall			Mean Luminal Diameter (µm)	Thrombosis
		Endothelium				Basement membrane				Hypertrophy	Part of wall	Entire Thickness of Wall at One Site One	Entire Circumference		
		Hyper- trophy	Disruption	Atrophy	Fibrinoid necrosis	Intact	Disrupted								
							One site	Two site	Multiple sites						
A (n = 25)	70 – 85	0	0	0	0	25	0	0	0	0	0	0	0	232.6	0
B (n = 11)	86 – 100	2	1	0	0	10	1	0	0	2	2	0	0	223.0	0
C (n = 24)	101 – 115	5	24	3	8	0	1	15	8	6	5	3	0	173.7	6
D (n = 15)	116 – 130	3	15	6	6	0	1	2	12	3	0	2	1	138.0	6

(100%) cases. It was disrupted at one site in one case (4%), at two sites in 15 (63%) cases and at multiple sites in eight cases (33%). In the tunica media, smooth muscles were hypertrophied in 10 (41.3%) placentae. In five placentae (20.8%), fibrinoid necrosis effected part of the wall of the spiral arteriole and in three cases it effected the entire thickness of the wall at one site (Fig. 1). The mean luminal diameter of spiral arteriole was 173.75 ± 9.64 µm (Fig. 2). Thrombi in the spiral arteriole were present in seven (29.1%) cases (Table 3).

In Group D, in the tunica intima, the endothelium was enlarged in three out of fifteen (20%) cases, was atrophic in six (40%), and underwent fibrinoid necrosis in six cases (48%). The basement membrane was disrupted at one site in one case (6%), at two sites in two (13%) cases and at multiple sites in 12 (80%) cases. In the tunica media, the smooth muscles were hypertrophied in twelve (80%) cases. Fibrinoid necrosis effected the entire thickness of the wall at one site in two (13.3%) placentae and full thickness of the wall in the entire circumference of the spiral arteriole underwent fibrinoid necrosis in one (6.6%) placenta (Fig. 1). The mean luminal diameter of the spiral arteriole was 168.07 ± 17.81 µm (Fig. 2). Thrombosis of spiral arterioles was present in

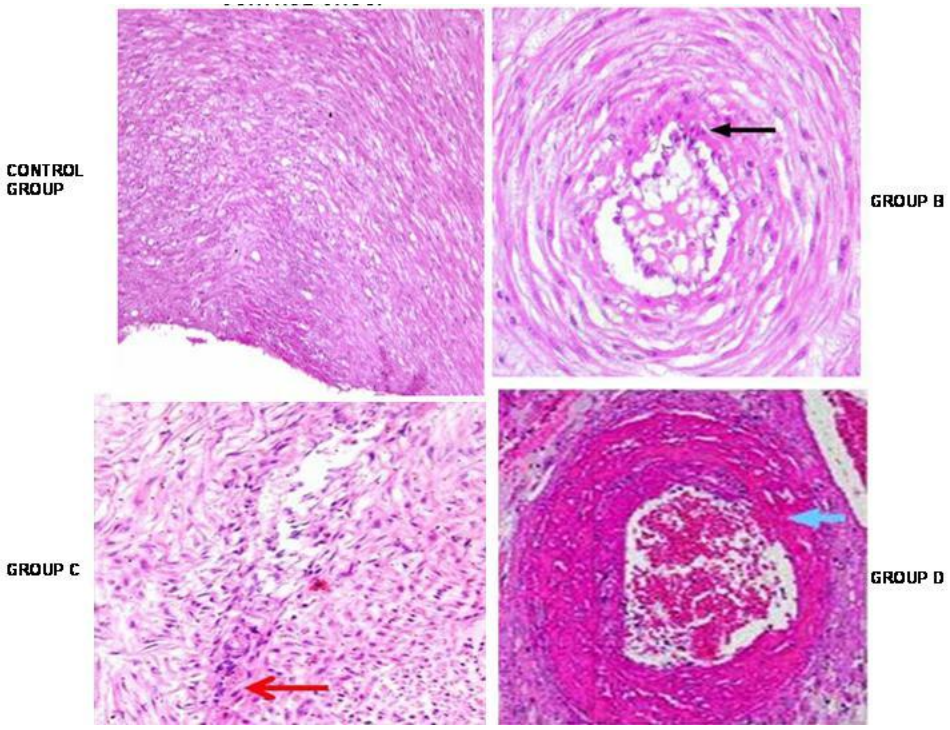

Fig. 1: *A photomicrograph of the maternal side of the placenta showing acomparison between fibrinoid necrosis in the wall of the spiral arteriole (H and E stain, Magnification 10 × 10 = 100X).*

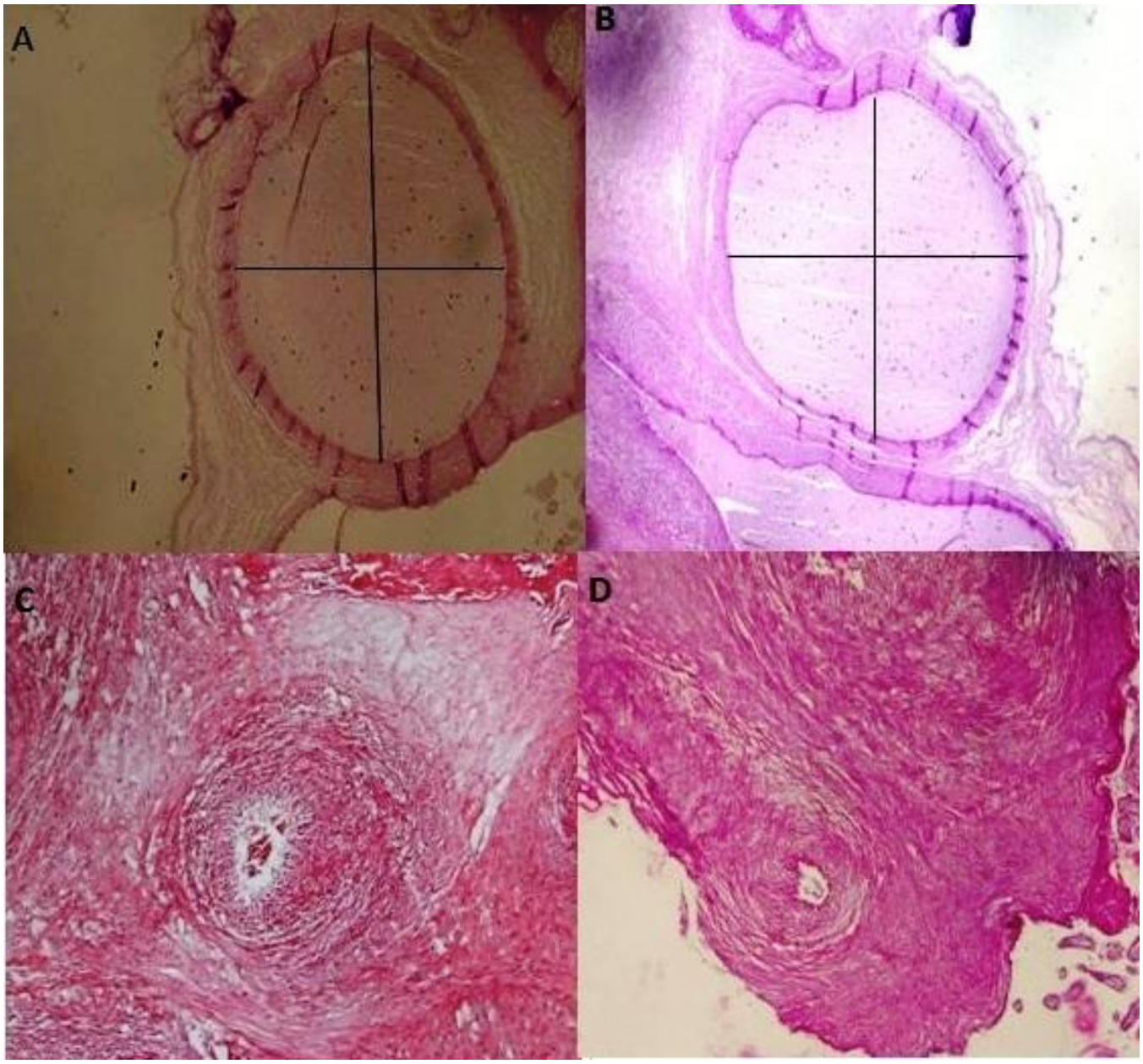

Fig. 2: *A photomicrograph of the histological section (A, control; B, C and D groups) of the maternal side of the placenta showing a comparison between the lumina of the spiral arterioles (H and E stain, Magnification 4 × 10 = 40 X).*

six (40%) of cases (Table 3).

Discussion

Pregnancy complications like preeclampsia are reflected in the placenta in a significant way both macroscopically and microscopically. Although placenta adapts itself to hypoxia, the compensatory changes are insufficient and result in a primary failure to develop and adequate placental mass.

The mean placental weight was significantly reduced in severe preeclamptic groups (Table 2). The minimum weight found in our study was 314.2 gms. These findings are in agreement with those of Meejus[17] who has reported a placental weight of 425 ± 111.2 gms in severe preeclampsia. As the severity of hypertension increases, placental weight decreases and the incidence of IUGR also rises.

The volume of placenta was significantly lowered in all three preeclamptic groups. Similar findings were observed by Majumdar[18] who mentions a volume of 375.9 cms with a mean diastolic blood pressure of 100 mm Hg.

In our study, the luminal diameter of spiral arterioles was decreased significantly in preeclamptic groups with mean diastolic blood preesure 108 and 123 mm Hg. Wolf[19]

mentions a luminal diameter of 128 µm with severe preeclampsia while another study mentions this diameter to be 112 µm with mean diastolic blood pressure of 110 mm Hg.[20] In preeclampsia, there is partial vascular adaptation of uteroplacental blood vessels which remain un-dilated. Hormone Leptin and placental cytokines increase significantly in preeclampsia and contribute to vasospasm.

The observed changes in endothelium were enlargement, atrophy, disruption and fibrinoid necrosis. Similar findings have been reported in earlier studies carried out by Nakamura, Hirabayashi and Muntefering.[21-23] These endothelial changes were accompanied by a disrupted basement membrane.[21,24] They were particularly significant in placentae of women with diastolic blood pressure 101 – 115 and 116 – 130 mm Hg and were also observed in mild preeclamptic group. In preeclampsia, disruption of basement membrane was attributed to a deposition of collagen like tissue in the basement membrane which compromises its strength and hence fails to with stand the mechanical pressure exerted by increased diastolic blood pressure.[25]

Hypertrophy of tunica media was a conspicuous feature in all three preeclamptic groups.An earlier study mentions hypertrophy of tunica media in severe preeclampsia with mean diastolic blood pressure 110 mm Hg.[26] This hypertrophy may be secondary to the development of hypertension and may act as a protective mechanism against high pressure.[26,27]

Fibrinoid necrosis of blood vessel wall (tunica intima and media) has been considered as a virtually pathognomonic lesion of preeclampsia.[28,29] It was believed to be the result of elevated blood pressure.[30] Some researchers are of the view that hypertension was not the cause of fibrinoid necrosis and suggested that an inappropriate immune reaction may be the causative factor.[31] Our data shows fibrinoid necrosis of blood vessel wall in all preeclamptic groups.

We observed thrombosis in the lumina of spiral arterioles in 29% placentae in group C and in 40% placentae in Group D (diastolic blood pressures 101 – 115 and 116 – 130 mm Hg respectively). These findings corroborated with the studies of other workers.[28,32] Salafia[28] in her study on 462 preeclamptic placentae and a wide range of blood pressure 90 – 105 mm Hg has reported thrombosis in 29% placentae. We attribute this difference in findings to the severity of hypertension in our groups.

The above mentioned pathologies in the spiral arterioles lead to a reduced blood supply and an altered morphometry of placenta resulting in IUGR and low birth weight of the baby.

Conclusion

The findings of this study suggest that mounting blood pressure adversely effects the gross morphology and histology of the maternal side of the placenta leading to uteroplacental ischemia.

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