**ORIGINAL ARTICLE**

# Histomorphometric Study of Umbilical Cord in Gestational Hypertension & Preeclampsia

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## ABSTRACT

**Aim:** To determine the effects of gestational hypertension alone & preeclampsia on the morphology & histology of umbilical cord.

**Methods:** 10 umbilical cords from normotensive patients & 10 each from gestational hypertension alone & preeclampsia were collected from Lady Wallingdon & Lady Aitchison Hospitals Lahore. The basis of selection and distribution of umbilical cords into groups was based on elevated diastolic blood pressure & proteinurea. The attachment, length, weight, diameter & color of cords was noted. On histological examination changes in its tunica intima & media were observed.

**Results:** there was change in the color & decrease in the length, weight of the cords with mounting blood pressure. Disruption of endothelium & basement membrane were present in both PIH groups. Both study groups showed hypertrophy of the wall & of tunica media but fibrinoid necrosis of the wall & luminal thrombosis was present in the preeclamptic group only.

**Conclusions:** From the study it was concluded that increase in pregnancy induced hypertension adversely affected the umbilical cord & hence the fetus

**Keywords:** pregnancy, hypertension, preeclampsia, umbilical cord, umbilical artery,

## INTRODUCTION

Umbilical cord in addition to acting as a mechanical conduit between the fetus & placenta also plays a role in the movement of blood & other substances between fetal & maternal circulation[1]. It normally contains two umbilical arteries & one umbilical vein[2]. These are embedded in a loose proteoglycan rich matrix known as Wharton's jelly which has an abundance of ground substance composed primarily of hyaluronic acid & very few fibers. The cells in this tissue are mainly fibroblasts[3,4].

It has been observed in various studies that there is decrease in thickness of umbilical cord in gestational hypertension & preeclampsia[5,6]. Gestational hypertension is defined as systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥90mmHg in a previously normotensive pregnant woman who is ≥20 weeks of gestation and has no proteinuria or new signs of end-organ dysfunction[7].

The blood pressure readings should be documented on at least two occasions at least four hours apart[8]. It is considered severe when sustained elevations in systolic blood pressure ≥160mmHg and/or diastolic blood pressure ≥110mmHg are present for at least four hours[9].

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Gestational hypertension is a temporary diagnosis for hypertensive pregnant women who do not meet criteria for preeclampsia. Preeclampsia (PE) is a pregnancy-specific syndrome[10] and it is characterized by the new onset of hypertension and proteinuria after the 20th week of gestation in women who previously were normotensive[11]. Although the estimated incidence of PE is 6–10% of all pregnancies in the United States, the incidence is believed to be even higher in underdeveloped countries[12]. Pre-eclampsia contributes significantly to maternal, foetal and neonatal morbidity and mortality[13]. PE increases the risk of later cardiovascular disease[14] and increases the overall risk of cancer[15]. In addition to the well-known maternal risk factors such as hypertension, diabetes mellitus, antiphospholipid antibody syndrome, obesity, aging, and multiple pregnancies, recent studies have identified the role of genetic and immunological factors in the pathogenesis of preeclampsia[16]. Pre-eclampsia is primarily, although not exclusively confined to the young women in their first pregnancy[17, 8].

## MATERIAL & METHODS

Ten specimens comprising of placentae & umbilical cords from women with normal pregnancies & twenty with pregnancy induced hypertension (PIH) were collected from the emergency labor rooms of Lady

Wallingdon Hospital & Lady Aitchison Hospital over a period of one year. Out of the 20 samples from PIH groups, ten sample each were from hypertension alone & ten with preeclampsia. Patients with a systolic blood pressure between 100-130mmHg & diastolic BP 60-80mmHg were labeled normotensive. Patient with a diastolic blood pressure >90mmHg without proteinurea & edema was allocated the Gestational hypertension group, & patient with a diastolic BP >90 with proteinurea fell into the preeclamptic group. Proteinurea was taken as 5 g. Of proteins in 24 hours urine specimen or 3+ on two random urine samples collected at least 4 hours apart. Fresh samples of umbilical cord were taken within two hours of delivery. The colour, length & site of attachment of the cord to the placenta were noted. The umbilical cord was cut along the clamp & the cord stump was measured at the same time. It was added in the cord length (from fetal to placental ends) for getting final length of the cord.

After separation of the cord from placenta its weight, diameter & number of arteries was noted. The blood vessels of the umbilical cord were flushed with normal saline followed by 10% normal saline. The labeled specimen were preserved & fixed in a labeled jar containing 10% formal saline for at least 24 hours. One cm thick sections were taken from each umbilical cord for processing in an automatic processor. 5 µm thick sections were cut from the distal, proximal & central portions of the umbilical cords & stained with haematoxylin & Eosin & Periodic Acid Schiff stain. On microscopic examination of the umbilical arteries, the integrity of endothelium & basement membrane the luminal diameter, wall thickness and any other pathology like fibrinoid necrosis was observed. Micrometry of the umbilical arteries was done. Heamatoxylin & Eosin stained sections of Wharthon's jelly were examined under microscope & number of fibroblasts / HPF were counted. All data was recorded on a specially designed proforma. Data analysis was done with SPSS version 15. Chi square & Pearson's Coefficient test were applied to analyze the data.

## RESULTS

The umbilical cords in Group "A" (normotensive patients) were examined for their attachment to the placenta, their number of blood vessels in cross section, color, weight, length & diameter were noted (Table 1). On microscopic examination, endothelium, basement membrane, tunica media of umbilical arteries were studied & the results were studied (Table 2 & 3). In Group B, (gestational hypertension without proteinurea) 8 out of 10 umbilical cords were attached centrally, one battledore & one was velamentous. Colour of 8 were pink & two were blue. All cords had one vein while one umbilical cord had single umbilical artery. On microscopic examination 80% of umbilical arteries showed intact endothelium, 20% showed disruption. Basement membrane was intact in 8 & disrupted in 2 umbilical arteries, tunica media of all the umbilical arteries showed hypertrophy (Table 2). Two umbilical arteries showed partial fibrinoid necrosis in their walls (Table 3). The maximum luminal diameter of umbilical arteries was 0.96 mm while minimum diameter was 0.80mm & mean diameter was 0.85±0.60mm. the maximum cellularity of Wharthon's jelly was 45 cells /PHF & minimum was 32 cells/ HPF. The mean cellularity was 38±4.5 cells /HPF (Table 1).

In Group C (preeclampsitic group) out of 10 umbilical cords, 7 were attached centrally, 2 were battledore & one was Velamentous. Colour of 7 umbilical cords were pink while 3 were blue. Each umbilical cord had a single vein while 2 cords had a single artery. Mean weight of umbilical cords was in this group was 38.9±0.87 g. the mean length of the umbilical cord was 51.6±2.01 cm while mean diameter of proximal, central & distal parts of umbilical cord were 2±0.23, 1.5 & 1.3±0.25cm respectively (Table 1). On microscopic examination 7 out of ten umbilical arteries showed intact endothelium, 7 displayed intact basement membrane (Table 2). All umbilical arteries showed hypertrophy of tunica media (Table 3). Mild thrombosis was noted in 3 umbilical arteries. Partial fibrinoid necrosis was seen in wall of 3 while complete fibrinoid necrosis was seen in one umbilical artery. The maximum wall thickness was 0.66 mm while minimum was 0.57 mm & mean thickness was 0.61±0.031. the maximum luminal diameter was 0.83 mm the minimum diameter 0.78 mm while the mean diameter was 0.8±0.017 mm. the cellularity of the Wharthon's jelly was reduced (Tables 2 & 3).

Table 1: Gross examination of Umbilical cord of different experimental Groups (B,C &D) with comparison to Control Group A

| Groups | Site of Attachment To placenta | | | Color of Umbilical cord | | Mean weight | Mean No. of Vessels | | Mean Length | Diameter (centimeters) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | C-Site | BD site | VM site | Pink | Blue | Grams | Veins | Arteries | Cm | P | C | D |
| A | 8 | 1 | 1 | 10 | 0 | 42.8 | 1 | 2 | 57.4 | 2.7 | 2.4 | 2.08 |
| B | 8 | 1 | 1 | 8 | 2 | 40.8 | 1 | 1.9 | 52.9 | 2.15 | 1.7 | 1.5 |
| C | 7 | 2 | 1 | 7 | 3 | 38.9 | 1 | 1.8 | 51.6 | 2.0 | 1.5 | 1.3 |

Key: UC: umbilical cord, C: central, BD: battledore, VM: velamentous, P: proximal, D: distal

Table 2: Histological changes in umbilical artery of the umbilical cord of different experimental groups with comparison with Control Group A

| Groups | Endothelium | | Basement membrane | |
|---|---|---|---|---|
| | Intact | Disrupted | Intact | Disrupted |
| A (n=10) | 10 | 0 | 10 | 0 |
| B (n=10) | 8 | 2 | 8 | 2 |
| C (n=10) | 7 | 3 | 7 | 3 |
| P value | 0.2 | 0.2 | 0.2 | 0.2 |

Table 3. Histological changes in Tunica Media, vessel wall, thrombosis & necrosis in umbilical arteries of umbilical cord of different experimental groups with comparison to the Control Group A.

| Groups | Tunica Media | | Wall | | Thrombosis | | | Fibrinoid Necrosis in the wall | |
|---|---|---|---|---|---|---|---|---|---|
| | Normal | Hypertrophy | Intact | Hypertrophy | Mild | Moderate | Severe | Partial | complete |
| A(n=10) | 10 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 |
| B(n=10) | 0 | 10 | 8 | 2 | 0 | 0 | 0 | 2 | 0 |
| C(n=10) | 0 | 10 | 7 | 3 | 3 | 0 | 0 | 3 | 1 |
| P value | 0.0001 | 0.2 | 0.0001 | 0.2 | 0.2 | 0 | 0.02 | 0.04 | 0.2 |

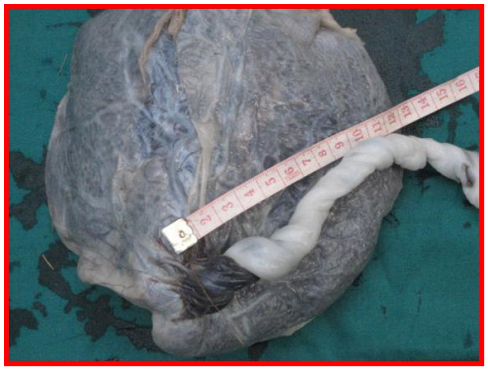

Fig 1: Gross picture of umbilical cord showing central attachment with placenta

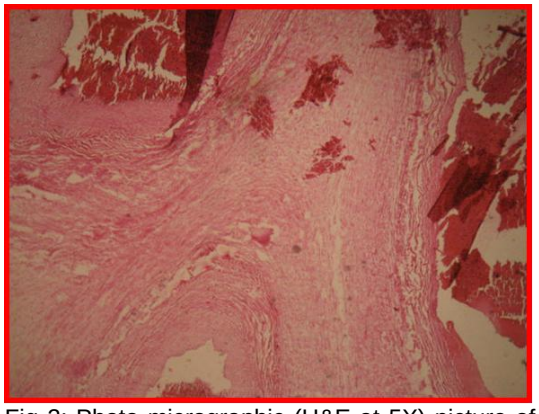

Fig 2: Photo micrographic (H&E at 5X) picture of umbilical cord showing vein, arteries and Wharton's jelly (Group A)

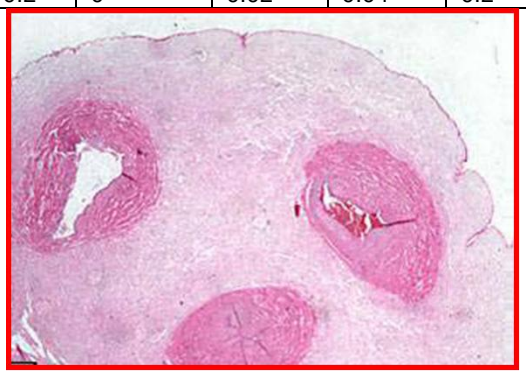

Fig 3: Photo micrographic (H&E at 5X) picture of umbilical cord showing vein, arteries and Wharton's jelly (Group B).

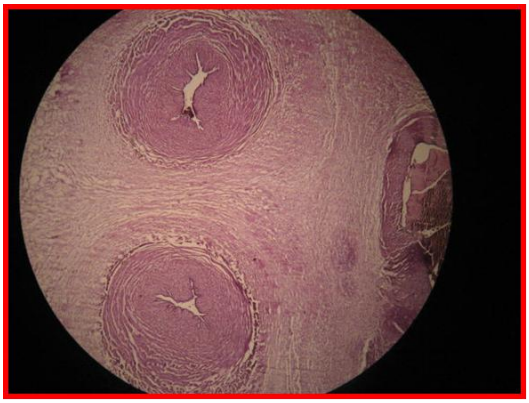

Fig 4: Photo micrographic (H&E at 5X) picture of umbilical vein, arteries and Wharton's jelly (Group C) with marked hypertrophy of wall and narrowing of luminal diameter for both arterial portion due to effect of PIH.

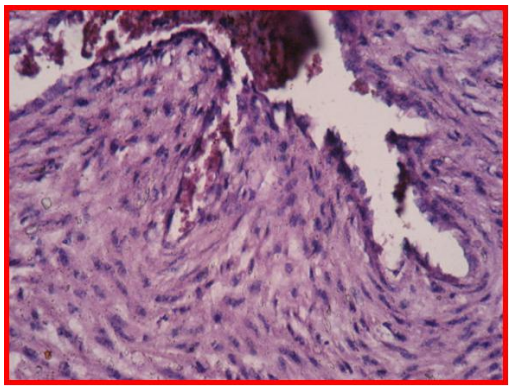

Fig 5: Photo micrographic (PAS at 40X) picture of umbilical Artery (Group D) with marked hypertrophy of wall with micro thrombi and necrosis disruption of endothelium and basement membrane (BM) for both arterial due to effect of PIH.

## DISCUSSION

PIH is a major contributor to maternal & fetal mortality morbidity & mortality[19,20]. Its complications are listed among the most common cause of maternal death in virtually all developed countries[21]. Preeclampsia is the most common pregnancy associated pathological syndrome accompanied by a significant increase in collagen & sulphated glycosaminoglycan (GAG's) content in umbilical arteries. The pathogenesis of preeclampsia is still not clear[22].

In this study the color of umbilical cords was significantly affected in PIH groups as compared to control groups (p 0.002) (Table 1) & indirectly it could be due to deficiency of NO as studied by Luzi et al & Harrington et al[23]. This hypothesis was almost similar to the findings of Zhang YN et al who claimed hypoxia was responsible for these changes.

The weight & length of the umbilical cord of the experimental group were effected but there was no significant statistical difference in the mean lengths & weights of these parameters in PIH groups versus control groups (p 1 .27 & 1.32 respectively). Our findings are consistent with Koesch et al who found reduction in weight & length of umbilical cord in patients suffering from PIH[24]. It has been suggested that deficiency of Ghrelin which has a potent growth hormone releasing with a dose dependent manner could be one of the factors. Experimental data suggests that Ghrelin may be an important link between nutrition & growth.

Attachment of umbilical cords with placenta (central, battledore & velamentous) was not significantly effected in PIH as compared to control Group A in our study. Ashfaq et al[25] presented similar findings in their study.

The reduction in diameter of the umbilical cord was significant in groups with PIH especially due to reduction in contents of Wharthon's jelly. This change was more pronounced at the distal end as compared to the proximal end & central area. Illie et al showed similar findings[26].

In PIH an umbilical vascular disorder was initially produced which was accompanied by increase in umbilical vascular resistance & reduction of the umbilical blood stream with a fetal hypo-perfusion.

Single umbilical artery is a relatively rare finding. In our study the number of arteries was also affected in the patients of PIH groups (Groups B & C) however the difference was not significant compared to the normal group (p=1.32). It cannot be concluded whether PIH is responsible for single umbilical artery or the single umbilical artery was the pathogenesis of PIH. It is claimed that single umbilical artery is associated with fetal malformations, IUGR & increased perinatal mortality in normal formed infants[27,28].

The umbilical arteries were also affected by PIH. Groups B & C compared to Group A with regards to structural changes in the umbilical blood vessels. Endothelium of both umbilical arteries showed similar changes. There was thickening of vessel wall, narrowing of lumen with thrombosis. Significant number of umbilical arteries showed hypertrophy of tunica media of wall of the artery (Group B & C p=0.0001 & 0.0001 respectively).

Fibrinoid necrosis of blood vessel wall has been considered as a virtually pathognomonic lesion of preeclampsia[29,30]. It was believed to be the result of elevated blood pressure[30]. We observed fibrinoid necrosis in Group C compared to A. Theories proposed for the formation of fibrinoid necrosis include precipitation & inspissation of fibrin or other blood derivatives, necrosis of collagen, coagulation of ground substance or a combination of these processes[31]. Our findings corroborated with those of other researchers[32]. The cellularity of Wharthon's jelly was significantly affected in all PIH groups in our study. Similar findings were reported by other researches who attributed these findings to placental ischemia which was the base of toxemia of pregnancy[33].

## CONCLUSION

PIH effected the morphology & histology of the umbilical cord in a major way. The colour & diameter of the umbilical cord were significantly affected. The weight & length of the cord was also effected but not to a significant extent. The histological changes were more significant in the preeclamptic group compared to the Group B (gestational hypertension without proteinurea).

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