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# Microscopic Estimation of the Volumes of Components of Umbilical Cord in Pregnancy Complicated with Hypertension

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**Abstract:**
**Context:** Clinically the adverse effects of hypertensive pregnancy are well established. Hypertensive pregnancies changes histological structures of umbilical cord which produce fetal and maternal complications. The present histological study was done to find out the area occupied by Wharton's jelly and total vessels area of umbilical cord in pregnancies complicated with hypertension. **Method:** This crosssectional, analytical study was done in the Department of Anatomy, Rangpur Medical College Rangpur from July 2014 to June 2015. The study was carried out on 60 (sixty) human umbilical cord, 30 from normotensive mothers (control group) and 30 from hypertensive mothers (hypertensive group). The umbilical cords were selected from Obstetric ward of Gynecology and Obstetrics Department, Rangpur Medical College Hospital, Rangpur after taking written permission. Area occupied by Wharton's jelly and total vessels area were measured microscopically by point counting method on prepared histological slides. **Result:** The mean (±SD) of proportional volume of area occupied by Wharton's jelly in placental side of umbilical cord was 82.00±1.46% and 68.55±7.49% and the mean (±SD) of proportional volume of Wharton's jelly area in fetal side of umbilical cord was 81.54±.78% and 71.28±6.01% in both control and hypertensive group respectively. The mean (±SD) of proportional volume of total vessels area in placental side of umbilical cord was 18.06±1.48% and 31.59±8.63% and the proportional volume of the mean (±SD) of total vessels area in fetal side of umbilical cord was 18.19±.70% and 28.64±5.98% in control and hypertensive group respectively. Whereas the jelly area was significantly decreased in hypertensive umbilical cord in both sides of the cord, the vessel area was significantly increased in hypertensive cord in both sides of the cord. **Conclusions:** Hypertension causes significant structural changes in umbilical cord that affects fetal and maternal wellbeing. So this study would be helpful for those who are concerned for mother and child health.

**Indexing words:** Umbilical cord, Hypertension, Volume component.

## Introduction:

The umbilical cord is a combination of blood vessels in which the tunica adventitial coat is formed by Wharton's jelly[1]. It is the nexus between the fetus and the placenta, thus umbilical vessels configuration may be an indicator of fetal status[2] and considered in understanding feto-maternal functional relationship and related clinical conditions[3].

Mucous connective tissue of Wharton jelly, present in the umbilical cord consists of a specialized, almost gelatin like extracellular matrix. It is largely made up of mucopolysaccharides (hyaluronic acid and chondroitin sulphate) and some fibroblast and macrophages[4]. It also contains cells with similar characteristics of smooth muscle ones and that allows its contractile functions[5, 6]. Wharton's jelly occupies large intercellular spaces located between thin, wispy collagen fibers. It is an important constituent of cord as it is the metabolically active tissue involved in exchange between amniotic fluid and umbilical vessels and is vital to the outcome of pregnancy. As a mucous tissue it protects and insulates umbilical

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blood vessels. Wharton's jelly, when exposed to temperature changes, collapses structures within the umbilical cord and thus provides a physiological clamping of the cord (an average of) 5 minutes after birth[7]. A reduction in the area of Wharton jelly resulting in a thin cord may cause restricted growth and low birth weight of the fetus[8].

Systemic diseases affecting mother can impose serious impacts on Wharton's jelly content thus affecting the cord architecture and finally the outcome of pregnancy. Hypertensive disorder of pregnancy is a leading cause of maternal and neonatal mortality and morbidity worldwide, particularly in developing countries, occurring in around 8% of pregnancies. These disorders causes intrauterine growth retardation due to utero-placental insufficiency and complications related to prematurity[9].

Microscopically the two umbilical arteries carry deoxygenated blood from fetus to mother, have a media composed of two muscle layers, an inner longitudinal and an outer circular. The internal elastic lamina is indistinct and missing in some places. A true adventitia is lacking in the segment within the umbilical cord[10]. One umbilical vein that passes through umbilical cord, carry oxygenated blood from placenta to fetus. Microscopically, umbilical vein larger in diameter, thin wall with single layer of disorganized circular smooth muscle and an internal elastic lamina[11].
Although the umbilical cord is one of the most vital components of the fetal anatomy, it is still one of the least studied fetal structures. Given that the umbilical cord is vulnerable to a number of abnormalities that may occur during pregnancy, labor, or delivery, it is important to investigate the underlying mechanisms of the development of cord morphology and possible pathologies associated with it, because this may provide insight regarding fetal growth within the intrauterine environment and its impact on later life[12].

**Methods:**

This cross- sectional analytical study was carried out on 60 (sixty) human umbilical cords. Out of the 60 umbilical cords, 30 were collected from normotensive mothers of uncomplicated pregnancies (control group) and 30 from mothers with hypertensive disorders of pregnancy (hypertensive group). Ethical clearance was taken from the Ethical Board of Rangpur Medical College. The umbilical cords were collected from Gynecology and Obstetrics Department, Rangpur Medical College Hospital, Rangpur after taking written permission. Umbilical cords of both normal vaginal and caesarian delivery were included. All samples were collected from singleton live pregnancy. Gestational period was between 35-42 weeks and maternal age within 20-45 years. An inclusion criterion for control group was **u**mbilical cord derived from mothers having blood pressure less than 140/90 mmHg. Inclusion criteria for hypertensive disorders group was umbilical cord derived from mothers having blood pressure 140/90 mmHg and above.

Common exclusion criteria were umbilical cord delivered from mothers with Rh negative blood group, VDRL positive, HBsAg positive, presence of any other known systemic pathology (diabetes mellitus, CLD, CVD, CKD and hematological disorders) and any congenital anomalies of the baby.

The samples were collected immediately after delivery and were examined for completeness in recent state. After then umbilical cord was cut 2 cm from the site of insertion. Then the umbilical cords and placenta were placed in 10% formalin filled plastic jar with cover for at least 7 days. Each jar was duly tagged with an identification number along with maternal name and BP. All the umbilical cords were collected and measured in similar manner.

For histological study, two tissue blocks were taken; one from placental end of cord, another from fetal end of cord. Slides were prepared following routine histological technique.

**Estimation of proportional volume of Wharton's jelly and Total vessels area**

The volume proportions of Whartons Jelly and blood vessels were determined by 'the point counting technique' for gross specimen described by Aherne and Dunnil (1966), proposed by Chalkley (1943-44)[13]. The principle depends on the fact that in a composite organ, the volumes of the components are equivalent numerically to the relative areas occupied by these components on cut surfaces. If a grid of regularly spaced points are placed over the cut surfaces, the number of points over these components will be proportional to their area, and hence, to their volume.
The proportion of volume of Wharton's jelly and total vessels area in the umbilical cord were determined with the replica of point counting Zeiss I integrating eyepiece prepared in a

transparent plastic sheet and was placed into the eyepiece. The integrating eyepiece contains a point network of 25 points, spaced at 70 µm, arranged within a circle which delimits the counting field.

The counting was done under light microscope (Olympus BX41, made in Japan) at low magnification (×10 objective ×10 eyepieces), in slides stained with routine H&E stain. The position of each point of grid, falling on any component of the Wharton's jelly and vessels areas was recorded for each field (Figure 1). Then the eyepiece was rotated and keeping the field constant and again the position of each point was recorded. Thus 50 points were recorded for each field. In this manner all the available fields were counted in both slides prepared from each cord. Total points were summated that hitting either Wharton's jelly area or vessels area and percentage of those was calculated. These percentages indicate the proportional volume of each component. The total number of points hitting each components of umbilical cord was summed up and expressed as a percentage. These percentage represents the proportional volume of the different components occupying the umbilical cord namely Wharton's jelly, umbilical arteries and vein.

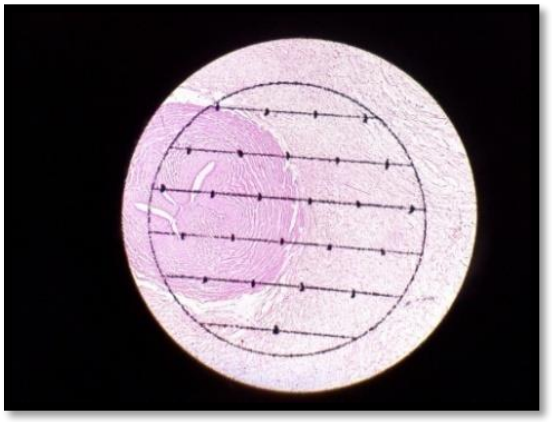


**Figure 1** Photomicrograph showing method of measurement of Wharton's jelly area and total vessels area by point counting method by a replica of Zeiss I integrating eyepiece.

**Result:**

Table 1 shows the mean (±SD) of proportional volumes of Wharton's jelly area in placental and fetal side of cord in control and hypertensive group.

It was observed that the mean (±SD) of proportional volume of area occupied by Wharton's jelly in placental side was 82.00±1.46% and 68.55±7.49% and 81.54±.78% and 71.28±6.01% in fetal side of the cord in control and hypertensive group respectively. The Wharton's jelly area were significantly lower in hypertensive group than in control group (p=.000) in both sides of the cord.

It could be revealed from the table that the area occupied by Wharton's jelly in both placental and fetal side was similar in control group but was somewhat reduced in placental side in hypertensive group than the fetal side (p>.05).

**Table 1:** Area occupied by Wharton jelly in placental side and fetal side of umbilical cord in control and hypertensive group (n=30in eachgroup)

| Variables | Groups | | p value |
|---|---|---|---|
| | Control | Hypertensive | |
| Wharton jelly area | 79.89 – 87.8 | 49.11 – 80.58 | .000(S |
| Placental side (%) | 82.00 ±1.46 | 68.55 ±7.49 | |
| Wharton jelly area | 79.37 – 83.5 | 58.62 – 82.24 | .000(S) |
| Fetal side (%) | 81.54 ±.78 | 71.28±6.01 | |

Results are shown as range and mean±SDs
p values reached from unpaired students t test
S: significant at 95% confidence level

Negative correlation was found between gestational age and Wharton's jelly in both fetal and placental side and reached a significant level in placental side only ($r^2$=.131, p=.049) in hypertensive group (Figure 2).

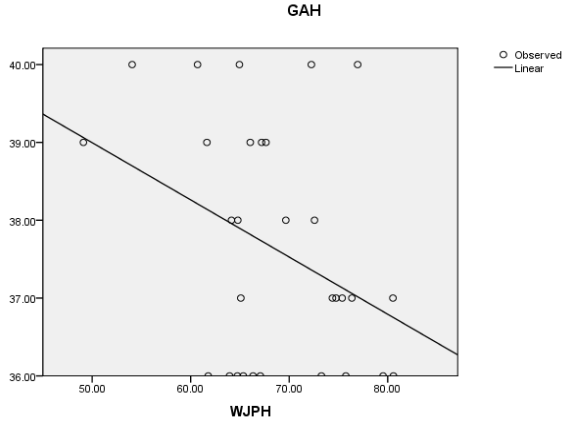



**Figure 2** Negative correlation between gestational age (GAH) and Wharton's jelly (WJPH) in placental side of hypertensive group ($r^2$ =.131, p =.049)

Regarding the proportional volume of vessel area, Table 2 shows the mean (±SD) of proportional volume of total vessels area in placental side of umbilical cord was 18.06±1.48% and 31.59±8.63% and in fetal side of umbilical cord was 18.19±.70% and 28.64±5.98% in control and hypertensive group respectively. The total vessel area was significantly higher in hypertensive group than in control group (p=.000).

Again it was observed from Table 2 that the mean of proportional volume of vessel area in placental side was more prominent in hypertensive group (p>.05) but in control group the mean value was similar.

**Table 2:** Area occupied by blood vessels in placental side and fetal side of umbilical cord in control and hypertensive group (n=30in eachgroup)

| Variables | Groups | | p value |
|---|---|---|---|
| | Control | Hypertensive | |
| Vessel area | 12.19 – 20.1 | 19.41 – 57.23 | .000 (S) |
| Placental side (%) | 18.06 ±1.47 | 31.59 ±8.63 | |
| Vessel area | 13.5 – 20.63 | 14.75 – 41.37 | .000 (S) |
| Fetal side (%) | 18.64 ± .70 | 28.64 ±5.98 | |

Results are shown as range and mean±SDs
p values reached from unpaired students t test
S: significant at 95% confidence level

**Discussion:**

It could be remembered that whereas the mean proportional volume of Wharton's jelly area in placental and fetal side (82.0±1. 46% vs 81.54±.779%) were similar in control group the mean value was somewhat lower in the placental side than fetal side (68.55±7.49%vs 71.28 ± 6.0%) in hypertensive group. But in both side of the cord, Wharton's jelly area was reduced significantly in hypertensive group than in control group. It was also found that there was significant negative correlation Wharton's jelly area and gestational age in hypertensive group (Figure 2).

Wharton's jelly consists of a fundamental amorphous substance containing glycosaminoglycans, proteoglycans and, predominantly, hyaluronic acid. It also contains cells with similar characteristics of smooth muscle ones and that, allows its contractile function. These cells constitute an interconnected network of collagen that form canaliculi and perivascular spaces permitting adequate blood flow to the fetus in cases of umbilical cord compression during pregnancy or delivery[14]. Wharton's jelly surrounds the umbilical vessels which constitutes the major part of human umbilical cord and provides a thick protective mantle around vessels[11].

Damasceno and de Lima[15] stated that the changes in the quantity or quality of Wharton's jelly affects the diameter of the umbilical cord and the hemodynamics of its vessels, leading to impaired fetal blood flow and consequently low weight gain and fetal demise. This constriction in the umbilical cord was due to the absence of Wharton's jelly that may be the cause of fetal death.

Barbieri et al[16] studied on a direct relationship between gestational age and the area of Wharton's jelly in the umbilical cord. There is an increase in the area of WJ as a function of gestational age until around 32 weeks, after which these measurements remain practically stable until the end of pregnancy. Findings of their study showed a positive and linear relationship between estimated fetal weight and the area of WJ, but only until the 26th week of gestational age, since then onwards there is almost no change in the area of WJ compared to estimated fetal weight.

Ilie et al[17] studied on Wharton's jelly, both qualitative and quantitative, found positive correlation with hypertension and intrauterine fetal growth restriction and establish pathogenic mechanisms for some groups of stillbirths.

Srivastava et al[7] studied on 60 umbilical cords. They found diameter of Wharton's jelly was smaller in hypertensive group than control group. They stated that if hypertension could be timely detected and properly managed, the complication of pregnancy and their adverse consequences can be avoided.

Reduction in the Wharton's jelly may be associated with single umbilical artery which may increase the rate of perinatal morbidity and mortality[18].

Milnerowicz et al[19] found thin cord with thinnest vessels and smaller content of Wharton's jelly in pregnancy induced hypertension results in IUGR.

Again, in the present study the proportional volume of vessel area was increased significantly in hypertensive than control group in

both placental (31.59±8.63% vs 18.06±1.47%) and fetal sides (28.64±5.98% vs18.19±.70%) of the cord. So it could be suggested that vessel area in the umbilical cord on both sides was increased in the expense of the amount of Wharton's jelly in the hypertensive group.

Again in the present study, the proportional volume of the vessel area in placental side of umbilical cord was similar to fetal side18.06±1.47% vs18.19±.70% in control group but vessel area was increased a little in placental side 31.59±8.63% vs 28.64±5.98% in hypertensive group.

The work of present study was done according to Bangal et al[20] but they found decrease in cord diameter but increase in total cord area in placental side in both control and PIH group. But in the present study the increase in vessel area and decrease in Wharton's jelly area was pronounced on both side of cord in hypertensive group than in control.

Inan et al[21] studied on comparative morphological difference between umbilical cords from chronic hypertensive and preeclamptic pregnancies. They stated that thickness of the umbilical cord vessels remained nearly constant, whereas both the total area and lumen area were reduced. These changes correlate with the histopathological findings, suggesting mainly vasocostrictive effect as a result of reduced uteroplacental perfusion followed by fetal hypoxia and intrauterine growth retardation in hypertensive pregnancy.

**Conclusion:**

Present study indicates that decrease Wharton's jelly area causes lean umbilical cord in hypertensive pregnant women and thickening of vascular wall causes obstructing feto-placental circulation leading to anoxia and fetal death. If Hypertension could be timely detected and properly managed, the complications of pregnancy and their adverse consequences can be avoided.

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