

HISTOMORPHOMETRIC ASSESSMENT OF WHARTON'S JELLY AREA IN NORMAL AND PRE-ECLAMPTIC PREGNANCIES AND ITS CORRELATION WITH PLACENTAL WEIGHT

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ABSTRACT

Introduction: Fetal capability to grow *in utero* depends on placental development and function. The goal of this study was to appraise the effects of hypertension on placental weight and Wharton's jelly area (WJA); and correlate them in normal and pre-eclamptic pregnancies.

Material and Methods: Eighty placentae along with umbilical cord divided into forty each of normotensive and pre-eclamptic pregnancies were studied. The cross-sectional area of the umbilical cord and vessels area was measured with the help of vernier scale and ocular micrometer respectively. WJA was calculated by deduction of the vascular area from the umbilical cord area. Placental weight was recorded by using a weighing machine and correlated with the WJA.

Results: In the present study, mean placental weight was 445.45 ± 40.31 grams and WJA was 35.28 ± 8.42 mm² in the normal group. Whereas, in the pre-eclamptic group, mean placental weight was 408.95 ± 47.15 grams and WJA was 29.04 ± 8.09 mm². Mean placental weight and WJA was significantly lower in the pre-eclamptic group. A significant positive correlation was found between WJA and placental weight ($r = 0.710$, $p < 0.0001$) in normal group and ($r = 0.764$, $p < 0.0001$) in pre-eclamptic group.

Conclusion: Pre-eclampsia is associated with reducing placental weight and WJA. Low WJA may hamper the fetal growth. The current study shows a strong positive correlation between WJA and placental weight. So, the awareness of this correlation will be helpful in the early observation of placental insufficiencies and provide sufficient information to take additional care in such conditions.

KEY WORDS: Wharton's jelly, Placental weight, Pre-eclampsia, Umbilical cord.

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INTRODUCTION

During intrauterine life, all the mandatory nutrients required for growth and development

of fetus passes through the placenta and umbilical cords. Therefore, proper examination of the placenta and umbilical cord gives an idea

about the fetal consequences when it was in the mother's womb.

Placenta undergoes different changes in structure, function, shape, and weight continuously, during its development throughout the gestation [1]. Complicated pregnancies like gestational diabetes or hypertension have an unhealthy impact on the placenta both macroscopically and microscopically. Pre-eclampsia is in concomitant with increase vascular resistance which may lead to reduce uteroplacental perfusion. As a result of decrease uteroplacental perfusion, fetal hypoxia and intrauterine growth retardation can become inescapable [2].

Fetal well-being depends upon the structure and function of the umbilical cord because fetomaternal blood flow is established by vessels within the cord. The umbilical cord vessels are cushioned by a special type of mucous connective tissue, known as Wharton's jelly, which is derived from the mucoid degeneration of primary mesodermal cells of the connecting stalk [3]. Wharton's jelly consists of the spongy network of interlacing collagen fibers that encases the umbilical vessels [4]. It contains myofibroblasts immersed in an extracellular matrix, primarily composed of glycosaminoglycans and proteoglycans [5]. The most abundant glycosaminoglycan is hyaluronic acid [6], which forms a hydrated gel around the collagen fibrils and maintains the tissue architecture of the umbilical cord [7]. So, the main function of Wharton's jelly is the protection of the umbilical blood vessels. Modifications in the composition of Wharton's jelly have been narrated in some pathological conditions such as fetal distress [8], maternal hypertension [9] and gestational diabetes [10]. Pre-eclampsia is associated with the reduced gelatinous activity, expression of insulin-like growth factor-1 binding protein [9] and cathepsin D activity [11]. In such pregnancies, Wharton's jelly areas are reduced as compared to normal pregnancies [12, 13].

The motive of this study was to evaluate the effects of hypertension on placental weight and area of the Wharton's jelly; and to determine the correlation between Wharton's jelly area and placental weight in both normal and pre-eclamptic pregnancies.

MATERIALS AND METHODS

The study was carried out in the Department of Anatomy and Department of Obstetrics and Gynaecology, Gandhi Medical College, Bhopal (M.P). Eighty placentae along with umbilical cord collected from pregnant women who delivered in Sultania Zanana Hospital associated with G.M.C. Bhopal, after informed consent and due permission from the institutional ethics committee. Women were diagnosed with preeclampsia if they had systolic BP ≥ 140 mmHg and diastolic BP ≥ 90 mmHg measured on two or more occasions at least 4 hrs apart after the 20th week of gestation with proteinuria [14]. Proteinuria was considered present when there was a urine dipstick value of at least 1+ (>30 mg/dl) on two separate occasions at least 6 hours apart. On this basis, subjects were divided into two groups. Group I consist of placentae along with umbilical cord obtained from normal pregnant women (n=40) with gestational age 37-40 weeks. Group II consisted of placentae along with umbilical cord obtained from pre-eclamptic women (n=40). Patients with diabetes mellitus, essential hypertension, renal disorders, anemia and other illness associated with pregnancy were excluded from this study.

The mothers and their neonates identified for this study were given code numbers and studied at the hospital. The placentae were collected soon after their expulsion and placental weight was recorded using the weighing machine. After delivery, appearance, pulse, grimace, activity, and respiration rate (APGAR) of the newborn was recorded.

In all cases, segments of umbilical cord were obtained at 2cm distance from the placental side, of the thickness of approximately 4-5 mm were routinely processed for paraffin embedding, sectioning, and H & E staining. Two diameters from each histological section of umbilical cord were measured at a right angle, by using vernier scale on the stage of the microscope. The diameters of each blood vessel cross section were obtained in the same way, but vessels diameters were done by an ocular micrometer.

Total cord area, Jelly area, and total vessel area were calculated for each cord by the formulae

given below:

1. $A = \pi D_1 D_2 / 4$ Where A is area and D is the diameter.
2. Total vessel area = (Total area of artery 1 + Total area of artery 2 + Total area of a vein) in cross-section.
3. Jelly area = (Total umbilical cord area - Total vessels area) in cross-section.

Standardizations of the methods: All measurements were taken by using a 4X magnification of the objective lens. The measurements which were taken from the vernier scale on the stage of the microscope, shows the real size of the sample because it is not affected by the magnification of the microscope.

The measurements which were taken by using ocular micrometer are the magnified value of the objective lens. The reticle is mounted in the eyepiece, which is magnified by the objective lens. Such as a real particle with a diameter of 1 mm at the microscope stage, when viewed with 4X objective lens will appear as 4mm diameter on the reticle. Hence such magnifications have to be taken into account while calculating real measurements.

Size of a sample displayed on reticle = Sample 'Real Size' X 'Magnification of Objective lens'

Statistical analysis of data was performed by using Statistical Package for Social Sciences (SPSS) version 15.0 (Chicago, IL). The values of continuous variables were presented as mean values \pm standard deviation. Correlation between the parameters was analyzed using Pearson's correlation coefficient. The significance of differences between group parameters was analyzed by Student's t-test and differences were considered significant if $p < 0.05$.

RESULTS

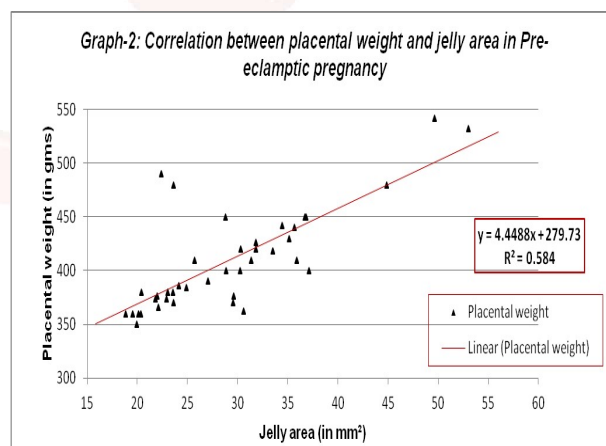
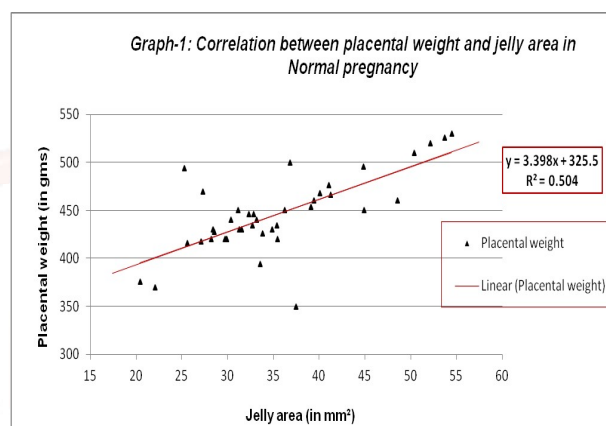
Gestational age was significantly lower in the pre-eclamptic group as compared to the normal group. In the normal group, mean placental weight was 445.45 grams, whereas in the pre-eclamptic group, mean placental weight was 408.95 grams. The mean placental weight was significantly lower in the pre-eclamptic group as compared to the normal group. In-turn, APGAR scores in the pre-eclamptic group were found to be significantly low [Table-1].

Table 1: Relationship of various parameters between normal and pre-eclamptic pregnancies.

S.No.	Parameters	Normal (n=40)	Pre-eclamptic (n=40)	P value ^a
1	Gestational age (weeks)*	38.02 \pm 1.32	36.17 \pm 0.93	0.0001 ^b
2	Placental weight (grams)*	445.45 \pm 40.31	408.95 \pm 47.15	0.0014 ^b
3	APGAR score*	8.07 \pm 1.07	6.6 \pm 0.98	0.0001 ^b
4	Wharton's jelly area (mm ²)*	35.28 \pm 8.42	29.04 \pm 8.09	0.0039 ^b

*Parameters were expressed as mean value \pm standard deviation;

- a. p-values were calculated by using Student's t-test. $p \leq 0.05$ was considered significant.
- b. Statistically significant.



Histomorphometric analysis of umbilical cord show mean Wharton's jelly area was 35.28 \pm 8.42 mm² in the normal group and 29.04 \pm 8.09 mm² in the pre-eclamptic group. WJA was significantly lower in the pre-eclamptic group as compared to the normal group [Table-1].

In the control group, there was a significant moderate positive correlation (Pearson correlation coefficient $r = 0.710$, $p < 0.0001$) between the placental weight and Wharton's jelly area. From the Graph-1, it is clear that the higher the value of the jelly area is associated with the higher the value of placental weight. The linear

relationship is expressed by the following equation:

$$y = 3.398 (x) + 325.5$$

Where x is the jelly area in mm² and y is the placenta weight in grams. The estimator of the slope is given by +3.398 gm/ mm² and the estimator of its intercept is given by +325.5 gm. The interpretation of the slope of the regression line is that on average, an increase jelly area of 10 mm² in control group is accompanied by an increase placental weight of 33.98 gm.

In the pre-eclamptic group, a significant strong positive correlation ($r = 0.764$, $p < 0.0001$) was found between placental weight and jelly area. For the pre-eclamptic group [Graph-2], the relationship between placental weight and the jelly area is given by the following equation:

$$y = 4.448 (x) + 279.7$$

Where x is the jelly area in mm² and y is the placental weight in grams. The estimator of the slope is given by +4.448 gm/ mm² and the estimator of its intercept is given by +279.7 gm. The interpretation of the slope of the regression line is that on average, an increase jelly area of 10 mm² in the pre-eclamptic group is accompanied by an increase placental weight of 44.48 gm. A test of linearity of the relationship between placental weight and the jelly area is statistically significant in both normal and pre-eclamptic group.

DISCUSSION

Placenta and umbilical cord being a fetal organ share the same stress and strain, to which the fetus is exposed during intrauterine life. Thus any disease process affecting the mother and fetus also has a great impact on placenta and umbilical cord [15]. Complicated diseases are metabolic in nature and they affect the placental efficiency and function. The feto-placental unit was adversely affected in pre-eclampsia. Due to placental insufficiency in pre-eclampsia, fetal growth was also affected [16]. *Das B. et al*, observed that Placental weight was significantly reduced where the duration of hypertensive disorders was prolonged. A significant increase in the incidence of intrauterine growth retardation and still birth was found with the lower placental weight [2]. In the present study, we found that mean placental weight were

significantly lower in the pre-eclamptic group [Table-1], which is similar to the observation of earlier researchers [17, 18].

Wharton's jelly is a metabolic active tissue involved in the exchange of metabolites and fluid between the umbilical vessels and the amniotic cavity [19]. It is composed of an insoluble fibrillar network of different collagen types within which soluble open-coil polysaccharides are held. Of these, the most represented is hyaluronic acid, which can entrap large amounts of water. A smaller part of the Wharton's jelly extracellular matrix is formed by sulfated glycosaminoglycans, which, in turn, are linked to proteins to form proteoglycans [6, 20]. *Bankowski et al*, showed that preeclampsia is accompanied by a significant increase in the ratio of sulfated glycosaminoglycans to hyaluronic acid. These findings suggest that the reduced amount of Wharton's jelly in preeclamptic women is characterized by reduced hydration due to less hyaluronic acid and more sulfated glycosaminoglycans [9]. The present study shows a significant reduction of Wharton's jelly area in the pre-eclamptic group [Table-1]. This finding is in-line with the study done by earlier observers [12, 13]. This reduction in Wharton's jelly area could be attributed to fetal starvation in the pre-eclamptic group as a result of poor maternal nutrition.

In the present study, we found a significant correlation between Wharton's Jelly area and placental weight in both groups [Graph - 1 & 2]. This indicates higher the value of Wharton's Jelly area is associated with higher the value of placental weight. This finding is similar to the *Filiz et al*, who reported that progressive increase in Wharton's Jelly is accompanied by an increase in placental weight [5]. *Di Naro et al* reported that diameters and areas of the umbilical cords changes during gestation, and these differences depend on the reduction of the amount of Wharton's Jelly [21]. The lean umbilical cords are accompanied by torsion and fibrosis of Wharton's jelly and thickening of the vascular wall which obstructs the feto-placental circulation, leading to anoxia and fetal death [22].

CONCLUSION

An important observation of the present study

is that placental weight and WJA were significantly decreased in the pre-eclamptic group and WJA was significantly correlated with placental weight in both groups. So, pre-eclamptic pregnancy produces a negatively impact on placental weight, which consequently produces a negative impact on the jelly area and perinatal outcomes. Awareness of this correlation will be helpful in the early assessment of placental sufficiency and state of fetal well being.

Conflicts of Interests: None

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