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Comparison of Wharton's Jelly Area in The Umbilical Cord Between Normal Pregnancies and Those with Preeclampsia in Relation to Birth Weight at Adam Malik Hospital and Hospitals within the University of North Sumatra Network

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Wharton's Jelly; Preeclampsia; Umbilical Cord; Birth Weight; Histomorphometry

ABSTRACT

Preeclampsia is one of the major complications of pregnancy that contributes significantly to maternal and fetal morbidity and mortality worldwide. This condition is associated with impaired placental function and fetal growth abnormalities, although the mechanisms underlying fetal growth restriction remain incompletely understood. Wharton's jelly, an extracellular matrix component of the umbilical cord, plays an important role in maintaining umbilical blood flow and protecting fetal circulation. This study aimed to compare the area of Wharton's jelly between normal pregnancies and preeclampsia pregnancies and to evaluate its relationship with infant birth weight. A comparative cross-sectional study was conducted involving 50 postpartum mothers, consisting of 25 preeclampsia cases and 25 normotensive pregnancies, at Adam Malik Hospital Medan, Prof. CPL USU Hospital, and Sundari Hospital Medan. Samples were collected using consecutive sampling, and measurements of umbilical cord morphology, Wharton's jelly area, placental characteristics, and infant birth weight were analyzed using appropriate statistical tests. The results showed that the Wharton's jelly area was significantly smaller in the preeclampsia group compared with the normotensive group ($p < 0.001$). Infants born to mothers with preeclampsia also had significantly lower birth weights ($p = 0.045$). Furthermore, Wharton's jelly area was positively correlated with birth weight in the normotensive group ($p = 0.014$; $r = 0.486$), but no significant correlation was observed in the preeclampsia group. In conclusion, reduced Wharton's jelly area is associated with preeclampsia and may contribute to differences in fetal growth outcomes. Further studies with larger populations and molecular approaches are needed to clarify its potential as a predictive biomarker for adverse pregnancy outcomes.

INTRODUCTION

Preeclampsia is a pregnancy disorder associated with hypertension, usually accompanied by proteinuria, that most often occurs after 20 weeks of gestation and is frequently diagnosed near the time of delivery. The disease represents a spectrum of hypertensive disorders of pregnancy, beginning with gestational hypertension and potentially progressing to more severe manifestations, such as eclampsia and HELLP syndrome. Preeclampsia accounts for 2%–8% of pregnancy-related complications, contributing to more than 50,000 maternal deaths and more than 500,000 fetal deaths worldwide (Erez et al., 2022; Macedo et al., 2020).

The incidence of preeclampsia is increasing worldwide, with a higher prevalence reported in developing countries compared with developed countries. According to the World Health Organization (WHO), the incidence of preeclampsia ranges from 2% to 10% of pregnancies globally. Approximately 1.8%–16.7% of cases are reported in developing countries, whereas the incidence in developed countries is approximately 0.4% (Khan et al., 2022). In Indonesia, the incidence of preeclampsia is estimated at 128,273 cases annually, accounting for approximately 5.3% of all pregnancies (Kasma et al., 2024). In North Sumatra, 3,560 cases of preeclampsia were reported among 251,449 pregnancies. Preeclampsia cases in North Sumatra Province contribute to 23.7% of maternal deaths and represent one of the five largest contributors to maternal mortality in Indonesia (Khodijah & Lumbanraja, 2021).

Hypertensive disorders of pregnancy are the second most common cause of perinatal morbidity and mortality. One of the associated morbidities is low birth weight (LBW) or impaired fetal growth, which may increase the risk of metabolic disorders later in life. Fetal growth disorders associated with impaired uteroplacental circulation include oligohydramnios, fetal growth restriction (FGR), and absent or reversed end-diastolic velocity (AREDV). Long-term effects may also occur in infants born to mothers with preeclampsia, including neonatal intensive care unit (NICU) admission, complications of prematurity, congenital heart disease, neurological developmental disorders, and other adverse outcomes (Ashraf et al., 2021).

Preeclampsia can affect birth weight. Numerous epidemiological studies have shown that women with gestational hypertension and preeclampsia contribute to a higher incidence of low birth weight (LBW) or small for gestational age (SGA) infants, and some studies have demonstrated that women with preeclampsia have a greater risk compared with those with gestational hypertension. Preeclampsia affects 3%–8% of all pregnancies and increases morbidity and mortality risks for both mothers and fetuses. In addition to increasing the risk of LBW, preeclampsia is associated with a higher risk of preterm birth, placental abruption, neonatal respiratory distress syndrome, cerebral palsy, and perinatal death. The etiology of preeclampsia is multifactorial, and the pathophysiological mechanisms underlying fetal growth restriction remain incompletely understood (Liu et al., 2021; Wu et al., 2019; Ferawati et al., 2023).

The umbilical cord connects the developing fetus to the placenta (Butureanu, 2025). It consists of two umbilical arteries, one umbilical vein, and an extracellular matrix (ECM) known as Wharton's jelly (Stefańska et al., 2020; Debebe et al., 2020). Changes in the umbilical cord, including fibrosis, may lead to constriction or hypercoiling of the cord (Kalluru et al., 2024; Dubetskyi et al., 2023), thereby impairing uteroplacental blood flow (Tonni et al., 2023; Hammad et al., 2020). The umbilical cord serves as the primary connection facilitating communication between the placenta and the fetus (Bohîlțea et al., 2022; Hayes et al., 2020). Embryologically, it develops from the extraembryonic mesoderm (Butureanu, 2025).

Fetal growth and development depend on the delivery of nutrients from the mother to the fetus through the placenta. Therefore, the size of the umbilical cord has the potential to predict fetal outcomes. Umbilical cord size affects umbilical venous oxygen levels, while umbilical arterial oxygen values are associated with birth size across the entire range of birth weights, in which oxygen availability serves as a major determinant of human fetal growth. Umbilical vein oxygen content is directly related to uteroplacental blood flow and placental diffusion capacity, which determine oxygen transport efficiency and can be considered a functional indicator of placental oxygen delivery. Meanwhile, umbilical artery oxygen content is inversely related to fetal oxygen consumption and, consequently, fetal growth as a major component of oxidative metabolism (Richardson et al., 2022).

A large umbilical cord may serve as a predictor of infant birth weight because it increases the risk of macrosomia, defined as a birth weight exceeding 4,000 g, by 20.6-fold and exceeding 4,500 g by 4.2-fold compared with infants with normal umbilical cord morphometry. A large umbilical cord has also been observed in macrosomic infants born to mothers with gestational diabetes mellitus. Conversely, a small umbilical cord (lean umbilical cord) is associated with a 4.4-fold increased risk of small for gestational age (SGA) infants compared with normal umbilical cord conditions. At gestational ages exceeding 25 weeks, this risk increases to 12.4-fold compared with normal umbilical cord measurements (Davies et al., 2021; Redline & Ravishankar, 2018).

Wharton's jelly is named after the English anatomist Thomas Wharton (1614–1673), who first described it in 1656. The fundamental components of Wharton's jelly include glycosaminoglycans, proteoglycans, and, particularly, hyaluronic acid. The elastic properties of Wharton's jelly are attributed to the combination of myofibroblasts and collagen types I, III, and V, which provide structural and contractile properties. The elasticity of the umbilical cord provides resistance to external pressure and functions as a physical buffer in regulating fetoplacental blood circulation and protecting central blood vessels. Wharton's jelly has multiple functions as a mucous connective tissue, including protecting and insulating the umbilical vessels. It provides a cushioning effect for umbilical cord blood vessels, ensuring that blood flow between the placenta and fetus is maintained within physiological limits and supporting fetal growth. When present in sufficient quantities, Wharton's jelly prevents umbilical cord compression and, immediately after birth, undergoes significant contraction, resulting in physiological clamping of the cord vessels within approximately 5 minutes and preventing substantial neonatal blood loss (Davies et al., 2021; Redline & Ravishankar, 2018).

Wharton's jelly is considered a supporting network that provides a perivascular and structural space, thereby maintaining adequate blood flow, preserving the anatomical integrity of the umbilical cord, and surrounding the umbilical vessels to prevent disruption of blood flow caused by compression or bending of the cord due to fetal movement or uterine contractions. The salt content of Wharton's jelly also participates in the regulation of umbilical blood flow; therefore, reductions in Wharton's jelly volume may contribute to umbilical vessel hypoplasia and fetal growth disorders (Butureanu, 2025). A prospective observational study conducted in the Department of Obstetrics and Gynecology, Kasturba Medical College, Manipal, Karnataka, India, over a two-year period analyzed the Wharton's jelly area using ultrasound in 250 women with a gestational age of 34 weeks who delivered within two weeks of the estimated date of delivery. Polynomial regression analysis demonstrated a strong correlation between Wharton's jelly area and birth weight ($R^2 = 0.8842$, $p < 0.001$) (Peyter et al., 2014; Nguyen et al., 2019).

However, research on umbilical cord morphology, particularly how the composition of Wharton's jelly changes in relation to infant birth weight and preeclampsia, as well as its role in disease progression, remains limited. Wharton's jelly is rich in collagen proteins and glycosaminoglycans (GAGs). In preeclampsia, a shift toward increased sulfated GAGs and decreased hyaluronic acid has been observed. This alteration in composition may indicate premature tissue aging that contributes to impaired fetal development. Nevertheless, limited information is available regarding changes in Wharton's jelly composition in fetuses with low birth weight (LBW), highlighting the need for further investigation. Jain Ankit et al. reported a significant positive correlation between Wharton's jelly area (WJA) and placental weight ($r = 0.710$, $p < 0.0001$) in the normal pregnancy group and ($r = 0.764$, $p < 0.0001$) in the preeclampsia group. Preeclampsia is associated with reduced placental weight and decreased WJA, and a low WJA may contribute to impaired fetal growth (Jain et al., 2019).

METHOD

Population and Research Sample

The population of this study was all women at Adam Malik Hospital Medan, Prof. CPL Hospital University of North Sumatra, and Sundari Hospital Medan. The research sample is a woman who has just given birth who meets the inclusion and exclusion criteria of the study. Sample collection is carried out by technique consecutive sampling.

Research Flow

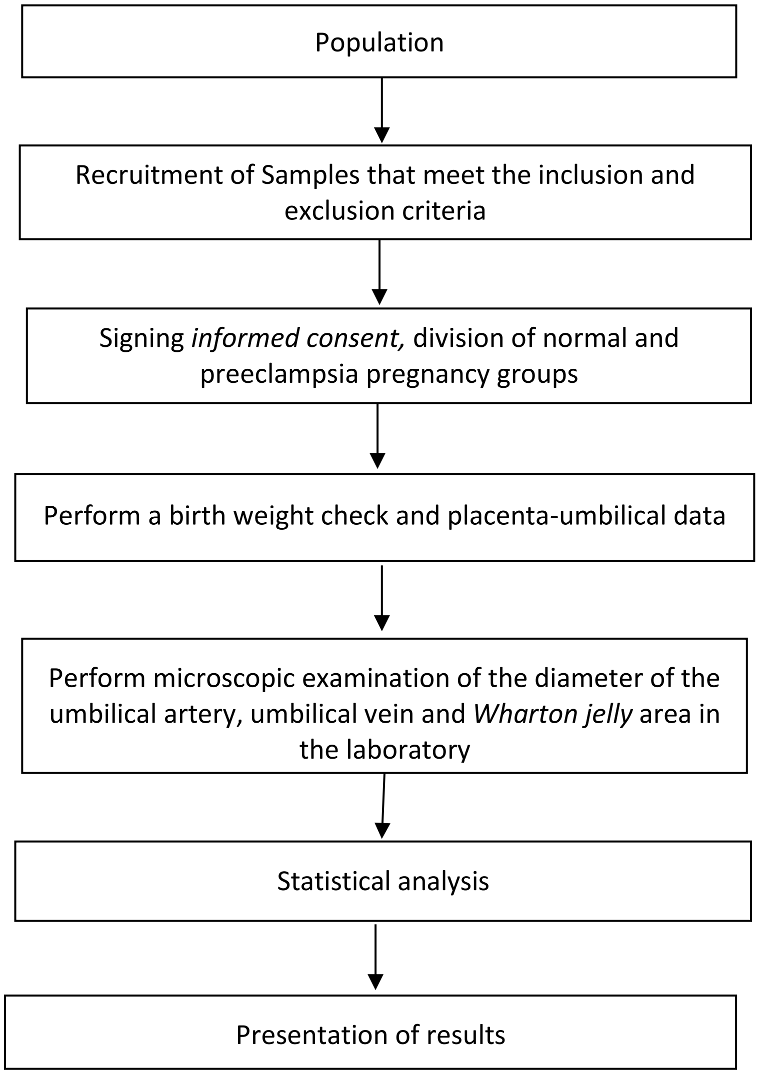

Figure 1. Research flow

RESULTS AND DISCUSSION

The Degree of Conformity of Placental Examination Results between Examiner I and Examiner II in the Maternal Group with Normotensive.

Table 1 compares the results of placental measurements in the mother with the normotension performed by two examiners (Examiner I and Examiner II). This analysis uses a statistical test *One Sample T Test* to test whether the average measurement difference between examiners is different or not statistically significant.

Table 1 Placental Examination Conformity Test between Examiner I and Examiner II in the Maternal Group with Normotension

Parameter	Range	Rerata ± SD	95% ME	*p value**
Placental Area, cm^2	0 – 59,69	2.39 ± 11.94	-2,54 – 7,32	0,327
Placental Thickness, cm	0 – 2	-0,02 ± 0,31	-0,15 – 0,11	0,746
Wharton Jelly Area, mm2	-0,44 – 34,56	1,4 ± 6,91	-1,45 – 4,26	0,320

**One Sample T Test*

The average value of the placenta area difference between examiners I and II was -2.39 ± 11.94 cm^2 with a *limit of agreement* of -2.54 – 7.32 cm^2. From the *one sample T test*, a value of p = 0.327 was obtained, meaning that there was no difference in the average area of the placenta between examiners I and II. In other words, there is an agreement between the results of the measurements of examiners I and II for the area of the placenta in the mother with normotension.

The average value of the difference in placenta thickness between examiners I and II was --0.02 ± 0.31 cm with *a limit of agreement* of -0.15 – 0.11 cm. From the *one sample T test*, a value of p = 0.746 was obtained, meaning that there was no difference in the average thickness of the placenta between examiners I and II. In other words, there is an agreement between the measurement results of examiners I and II for placental thickness in mothers with normotension.

The average value of *the Wharton jelly* area difference between examiners I and II was 1.4 ± 6.91 mm^2 with a *limit of agreement* of -1.45 – 4.26 mm^2. From the *one sample T test*, a value of p = 0.320 was obtained, meaning that there was no difference in the average area *of Wharton jelly* between examiners I and II. In other words, there is an agreement between the measurement results of examiners I and II for the area of *Wharton jelly* in mothers with normotonic.

Suitability of Arterial and Umbilical Vein Examination Results between Examiner I and Examiner II in the Maternal Group with PE

Table 2 compares the results of diameter and area measurements of the arteries and umbilical veins in mothers with Preeclampsia performed by two examiners. This analysis uses a statistical test *One Sample T Test* to test whether the average measurement difference between examiners is different or not statistically significant.

Table 2. Umbilical Vascular Examination Conformity Test between Examiner I and Examiner II in the Maternal Group with PE

Parameter	Range	Rerata ± SD	95% I	*p value**
Diameter Arteri A, mm	0 – 0,15	0,01 ± 0,03	-0,01 – 0,02	0,327
Artery Area A, mm^2	0 – 0,45	0,02 ± 0,09	-0,02 – 0,06	0,327
Diameter Arteri B, mm	-0,03 – 0,09	0,002±0,02	-0,01 – 0,01	0,546
Artery Width B, mm^2	-0,09 – 0,21	0,01 ± 0,05	-0,01 – 0,02	0,619
Diameter Vena, mm	-1,04 – 0	-0,04 ± 0,21	-0,13 – 0,04	0,327
Vein Area, mm2	-3,82 – 0	-0,15 ± 0,76	-0,47 – 0,16	0,327

**One Sample T Test*

The mean difference in the diameter of umbilical artery A between Examiners I and II was 0.01 ± 0.03 mm, with a *limit of agreement* ranging from −0.01 to 0.02 mm. Based on the *one-*

sample t-test, a *p*-value of 0.327 was obtained, indicating that there was no significant difference in the mean diameter of umbilical artery A between Examiners I and II. In other words, the measurement results of Examiners I and II demonstrated agreement regarding the diameter of umbilical artery A in mothers with preeclampsia.

The mean difference in the area of umbilical artery A between Examiners I and II was 0.02 ± 0.09 mm², with a *limit of agreement* ranging from −0.02 to 0.06 mm². Based on the *one-sample t-test*, a *p*-value of 0.327 was obtained, indicating that there was no significant difference in the mean area of umbilical artery A between Examiners I and II. Therefore, the measurement results of Examiners I and II demonstrated agreement regarding the area of umbilical artery A in mothers with preeclampsia.

The mean difference in the diameter of umbilical artery B between Examiners I and II was 0.002 ± 0.02 mm, with a *limit of agreement* ranging from −0.01 to 0.01 mm. Based on the *one-sample t-test*, a *p*-value of 0.546 was obtained, indicating that there was no significant difference in the mean diameter of umbilical artery B between Examiners I and II. Thus, the measurement results of Examiners I and II demonstrated agreement regarding the diameter of umbilical artery B in mothers with preeclampsia.

The mean difference in the area of umbilical artery B between Examiners I and II was 0.01 ± 0.05 mm², with a *limit of agreement* ranging from −0.01 to 0.02 mm². Based on the *one-sample t-test*, a *p*-value of 0.619 was obtained, indicating that there was no significant difference in the mean area of umbilical artery B between Examiners I and II. Therefore, the measurement results of Examiners I and II demonstrated agreement regarding the area of umbilical artery B in mothers with preeclampsia.

The mean difference in umbilical vein diameter between Examiners I and II was −0.04 ± 0.21 mm, with a *limit of agreement* ranging from −0.13 to 0.04 mm. Based on the *one-sample t-test*, a *p*-value of 0.327 was obtained, indicating that there was no significant difference in the mean diameter of the umbilical vein between Examiners I and II. Therefore, the measurement results of Examiners I and II demonstrated agreement regarding the diameter of the umbilical vein in mothers with preeclampsia.

The mean difference in umbilical vein area between Examiners I and II was −0.15 ± 0.76 mm², with a *limit of agreement* ranging from −0.47 to 0.16 mm². Based on the *one-sample t-test*, a *p*-value of 0.327 was obtained, indicating that there was no significant difference in the mean area of the umbilical vein between Examiners I and II. Therefore, the measurement results of Examiners I and II demonstrated agreement regarding the area of the umbilical vein in mothers with preeclampsia.

Degree of Conformity of Placenta Examination Results between Examiner I and Examiner II in the Group of Mothers with Preeclampsia

Table 3 compares the results of placental measurements in mothers with Preeclampsia conducted by two examiners (Examiner I and Examiner II). This analysis uses a statistical test *One Sample T Test* to test whether the average measurement difference between examiners is different or not statistically significant.

Table 3. Placental Examination Suitability Test between Examiner I and Examiner II in the Group of Mothers with Preeclampsia

Parameter	Range	Rerata ± SD	95% I	*p value**
Placental Area, cm^2	0 – 27,49	1,10 ± 5,50	-0,12 – 0,12	0,327
Placental Thickness, cm	-1 – 1	0 ± 0,29	-0,12 – 0,12	1,000
Wharton Jelly Area, mm2	-14,92 – 3,82	-1,06 ± 4,23	-2,81 – 0,68	0,221

**One Sample T Test*

The average value of the difference in placenta area between examiners I and II was -1.10 ± 5.50 cm^2 with a *limit of agreement* of -0.12 – 0.12 cm^2. From the *one sample T test*, a value of p = 0.327 was obtained, meaning that there was no difference in the average area of the placenta between examiners I and II. In other words, there is a suitability of the results of the measurements of examiners I and II for the area of the placenta in the mother with PE.

The average value of the placenta thickness difference between examiners I and II was 0 ± 0.29 cm with *a limit of agreement* of -0.12 – 0.12 cm. From the *one sample T test*, a value of p = 1,000 was obtained, meaning that there was no difference in the average thickness of the placenta between examiners I and II. In other words, there is an agreement between the results of the measurement of examiners I and II for placental thickness in mothers with PE.

The average value of *the Wharton jelly* area difference between examiners I and II was -1.06 ± 4.23 mm^2 with a *limit of agreement* of -2.81 – 0.68 mm^2. From the *one sample T test*, a value of p = 0.221 was obtained, meaning that there was no difference in the average area *of Wharton jelly* between examiners I and II. In other words, there is an agreement between the measurement results of examiners I and II for the area of *Wharton jelly* in mothers with PE.

Differences in Placenta Characteristics and Thickness *Wharton jelly* on the Umbilical Cord between Normal Pregnancy and Preeclampsia

Table 4 compares the characteristics of the umbilical cord, the structure of the umbilical cord blood vessels (arteries and umbilical veins), as well as the characteristics of the placenta and the thickness *of Wharton jelly* between pregnancy with preeclampsia and normal pregnancy at Adam Malik Hospital Medan, Prof. CPL USU Hospital and Sundari Hospital Medan.

Table 4. Differences in Placenta Characteristics and Thickness *Wharton jelly* on the Umbilical Cord between Preeclampsia and Normal Pregnancy

Parameter	Preeclampsia (n=25)	Normotensive (n=25)	p
Countersting			
Length (cm)	47,6 ± 7,08	42 (35 – 70)	0,092a
Diameter (mm)	9 (8 – 10)	10 (10 – 12)	<0,001a
Area(mm2)	63,62 (50,27-78,54	78,54 (78,54-113,1)	<0,001a
PD. Umbilical			
Diameter Arteri A, mm	1,84 (1,35 – 3,47)	1,79 (1,35 – 3,08)	0,816a
Artery Area A, mm^2	2,65 (1,43 – 9,46)	2,52 (1,43 – 7,44)	0,816a
Diameter Arteri B, mm	1,91 (1,4 – 3,78)	2,17 (1,23 – 4,13)	0,655a
Artery Width B, mm^2	2,85 (1,53 – 11,25)	3,7 (1,18 – 13,42)	0,655a
Diameter Vena, mm	2,81 ± 0,76	2,83 (2,21 – 5,05)	0,377a

Vein Area, mm2	6,19 (2,05-19,53)	6,3 (3,84-20,05)	0,377a
Wharton Jelly Area, mm2	52,12 ± 9,18	67,45 (56,47-104,16)	<0,001a
Placenta			
Placental Area, cm^2	250,73 ± 46,66	263,44 ± 69,17	0,492b
Placental Thickness, cm	1,5 (1 – 3)	2 (1 – 3)	0,095a

The data was presented with an average of ± elementary and median (min – max)
aMann Whitney, bT Independent

Based on cord size, there was no significant difference between the preeclampsia and normal groups (47.6 ± 7.08 cm vs 42 cm [range 35–70]; p = 0.092). The diameter of the umbilical cord in the preeclampsia group was smaller (9 mm [range 8–10]) than in the normal group (10 mm [range 10–12]; p < 0.001). The umbilical cord area in the preeclampsia group was also smaller (63.62 mm² [range 50.27–78.54]) than in the normal group (78.54 mm² [range 78.54–113.1]; p < 0.001).

Based on cord blood vessels, it was found that there was no significant difference in the diameter or area of arteries A and B between the two groups (p > 0.05). For measures of umbilical vein diameter (2.81 ± 0.76 mm vs 2.83 mm [range 2.21–5.05]; p = 0.377) and venous area (6.19 mm² [range 2.05–19.53] vs 6.3 mm² [range 3.84–20.05]; p = 0.377) did not differ statistically.

Based on placental area size, there was no significant difference between the preeclampsia and normal groups (250.73 ± 46.66 cm² vs 263.44 ± 69.17 cm²; p = 0.492). Meanwhile, for placental thickness, placenta thickness tended to be thinner in the preeclampsia group (1.5 cm [range 1–3]) than in the normal group (2 cm [range 1–3]), but did not differ significantly (p = 0.095).

Based on the size of *the Wharton jelly area,* it was found that the area *of Wharton jelly* in the preeclampsia group was smaller (52.12 ± 9.18 mm²) than in the normal group (67.45 mm² [range 56.47–104.16]. Using the Mann Whitney test, it was shown that there was a significant difference in *the size of Wharton jelly's area* between the group of mothers with Preeclampsia and the group of normotensive mothers.

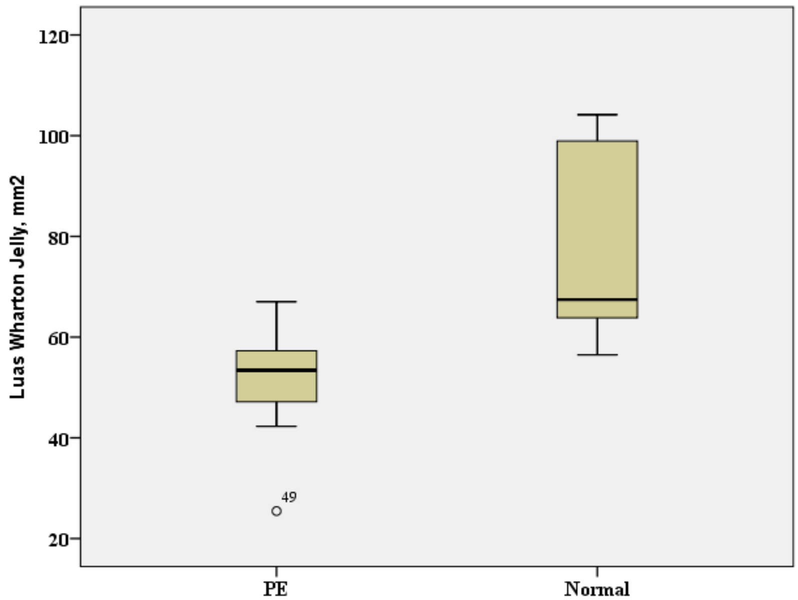

Figure 2. Wide Differences *Wharton jelly* between the Maternal Group with Preeclampsia and the Maternal Group with Normotensive

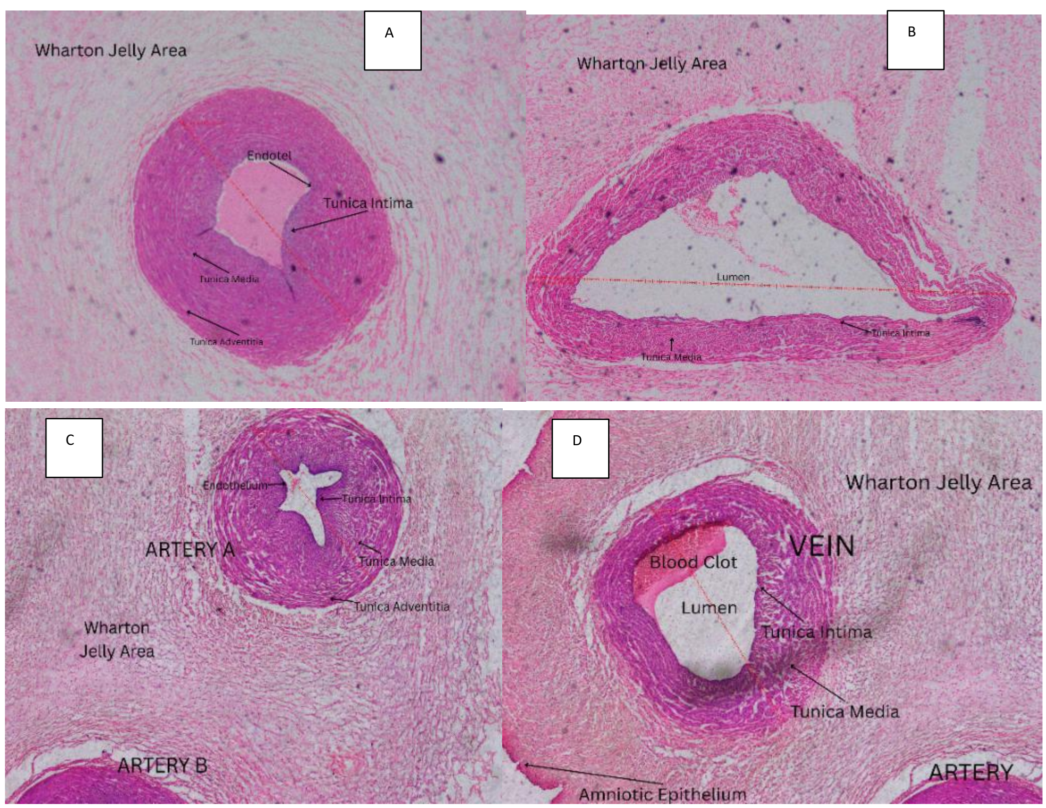

Figure 3. Microscopic Picture of Haematoxylin-Eosin-stained blood vessels in Normal Pregnancy and Preeclampsia. (a) normal arteries, (b) normal veins, (c) preeclampsia arteries, (d) preeclampsia veins. 30x magnification.

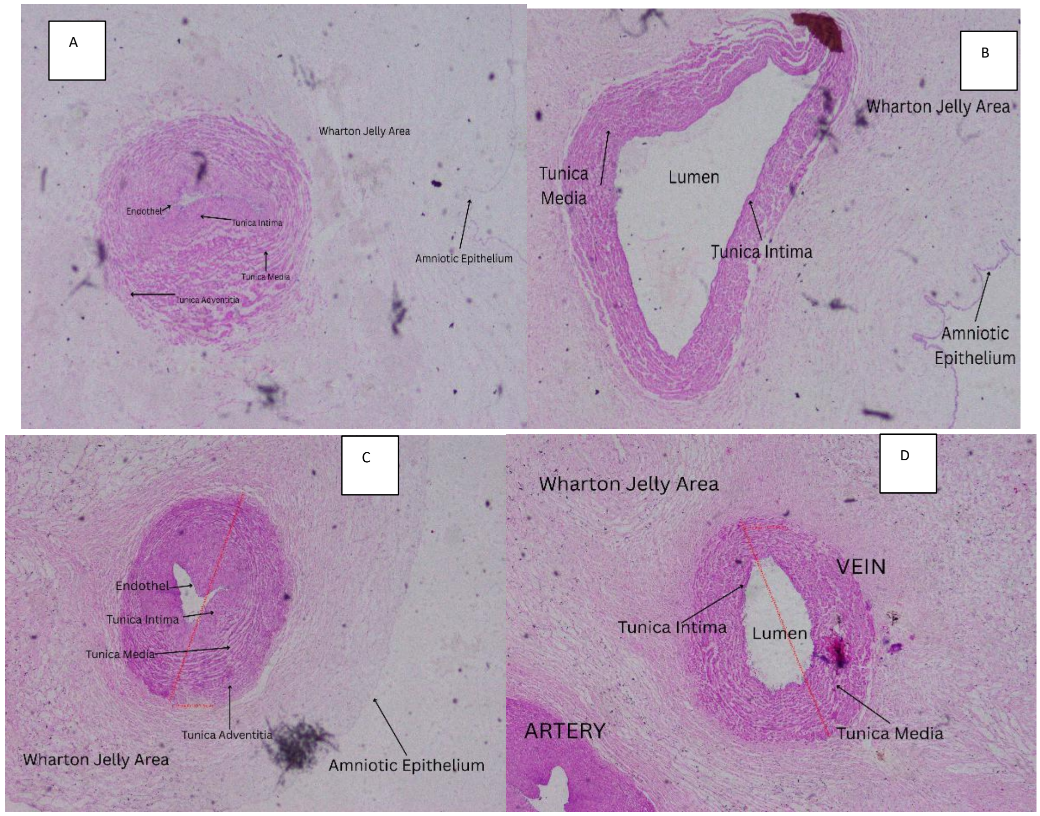

Figure 4. Microscopic Picture of PAS-stained blood vessels (*Periodic Acid Schiff)* in Normal Pregnancy and Preeclampsia. (a) normal arteries, (b) normal veins, (c) preeclampsia arteries, (d) preeclampsia veins. 30x magnification.

Difference in Baby Size from Mothers with Normal Pregnancy and Preeclampsia

Table 5 compares the size of the baby (birth weight and body length) between preeclampsia and normal pregnancy at Adam Malik Hospital Medan, Prof CPL USU Hospital, and Sundari Hospital Medan.

Table 5. Difference in Baby Size from Mothers with Normal Pregnancy and Preeclampsia

Parameter	Preeclampsia (n=25)	Normotensive (n=25)	p
Infant Birth Weight, grams	3046,4 ± 599,4	3347,6 ± 420,33	0,045a
Baby Body Length, cm	47,38 ± 2,29	47 (45 – 53)	0,563b

The data was presented with an average of ± elementary and median (min – max)
aT Independent, b Mann Whitney

The average birth weight of babies in the Preeclampsia group was 3,046.4 ± 599.4 grams. Meanwhile, the group of mothers with normotension had a higher average birth weight of 3,347.6 ± 420.33 grams. Using the T Independent test, a $p<0.05$ value was obtained, this difference is statistically significant.

The average body length of a baby from a mother with Preeclampsia is 47.38 ± 2.29 cm while in babies from mothers with normotension with a median of 47 cm. No significant differences in body length were found between infants from mothers with Preeclampsia and normotension (p=0.563).

Size Relationship *Wharton jelly* with Birth Weight of Babies from Mothers with Preeclampsia and Normocytes Mothers

Table 6 presents an analysis of the relationship between placental characteristics, umbilical vessel structure, and *Wharton jelly thickness* with infant birth weight in preeclampsia pregnancy and normal pregnancy (normotension) at Adam Malik Hospital Medan, Prof. CPL USU Hospital, and Sundari Medan Hospital. This analysis used the Pearson correlation test for normally distributed data and Spearman for normally distributed data, to evaluate the morphological influence of the umbilical cord and placenta on fetal growth.

Table 6. Placental Connection, Umbilical Blood Culvert and *Wharton jelly* with Birth Weight of Babies from Mothers with Preeclampsia and Normocytes Mothers

	Birth Weight			
Parameter	Preeclampsia		Normotensive	
	p	r	p	r
Wharton *jelly*	0,156a	-0,293	0,014b	0,486
Placenta Area	0,183a	0,275	0,450b	0,158
Umbilical Artery A Area	0,741b	0,070	0,412b	0,172
Umbilical Artery Width B	0,406b	0,075	0,072b	-0,366
Umbilical Vein Area	0,720b	-0,275	0,027b	-0,442
Placenta Thickness	0,109b	0,328	0,895b	0,028

aPearson , bSpearman

Analysis of the correlation between placental characteristics, umbilical cord vascular structure, and *Wharton jelly* with infant birth weight showed different variation in preeclampsia and normotension pregnancy groups. In the preeclampsia group, *the extent of Wharton jelly* showed no significant association with infant birth weight (p = 0.156; r = -0.293). In contrast, in the normotension group, *Wharton jelly* area was positively and significantly correlated with infant birth weight (p = 0.014; r = 0.486), indicating that this tissue thickness supports optimal fetal growth through mechanical protection and regulation of blood flow. The correlation value obtained was 0.486, meaning that there was a positive correlation or any increase in *the area of Wharton jelly* would be followed by an increase in the baby's birth weight in mothers with normotension with moderate strength levels (r-value = > 0.4 – 0.6).

When observing placental area, no significant correlation was found in either group, either in preeclampsia (p = 0.183; r = 0.275) or normotension (p = 0.450; r = 0.158). From the analysis of placental thickness, it also showed no significant association with the baby's birth weight in the PE group and the normotonic maternal group.

In umbilical vessels, the area of the umbilical artery A and the umbilical artery B did not correlate with birth weight in both preeclampsia (p = 0.741; r = 0.070) and (p = 0.406; r = 0.075) and normotension (p = 0.412; r = 0.172) and (p = 0.072; r = -0.366). Meanwhile, umbilical vein area was not correlated in the preeclampsia group (p = 0.720; r = -0.275), but showed a significant negative correlation in the normotension group (p = 0.027; r = -0.442). Negative values indicate that there is an inverse correlation between the area of the umbilical vein and the birth weight of the baby, the smaller the area of the umbilical vein will be followed by an increase in the baby's birth weight or the larger the area of the umbilical vein, it will be followed by a decrease in the baby's birth weight. The level of force produced between the umbilical vein and the infant's birth weight was moderate ($r = > 0.4 – 0.6$).

Analysis of the Characteristics of Preeclampsia and normotension cases

Among the 25 subjects with preeclampsia, the mean maternal age was 30.2 ± 6.46 years, whereas among the 25 normotensive subjects, the mean age was 28.88 ± 5.26 years. These findings indicate that the normotensive subjects were younger than the subjects with preeclampsia. In the preeclampsia group, the most common gestational age was 38 weeks, accounting for 52% of the 25 subjects, while in the normotensive group, the most frequent gestational age was 39 weeks, accounting for 40% of the 25 subjects. In the preeclampsia group, 14 out of 25 subjects (56%) were primigravida, whereas 10 out of 25 subjects (40%) were multigravida.

In the preeclampsia group, the most common mode of delivery was cesarean section, occurring in 21 out of 25 subjects (84%). This finding is consistent with the study by Pasokpuckdee et al., who conducted a retrospective study involving 62 patients with preeclampsia over a three-month period and reported a significant increase in the overall rate of cesarean section (RR = 1.8, $p < 0.001$) (Pasokpuckdee & Boriboonhirunsarn, 2023). This result is also consistent with the findings of Sukmawati et al., who reported that during a 2.5-year study of preeclampsia cases, among 329 mothers with preeclampsia, 24.3% underwent vaginal delivery, whereas 75.7% underwent cesarean section (Sukmawati et al., 2020). Based on birth weight data, the mean birth weight of infants in the preeclampsia group was 3,046.4 ± 599.4 g. Meanwhile, the normotensive group had a higher mean birth weight of 3,347.6 ± 420.33 g. An independent t-test yielded a p-value < 0.05, indicating that this difference was statistically significant. These findings are also consistent with the study by Gan Bei et al., which reported that among 333 cases of preeclampsia, the median birth weight was 2,800 g (2,100–3,500 g), which remained within the normal birth weight category (Gan et al., 2022).

Analysis of Differences in Placenta Characteristics and *Wharton Jelly Thickness* in the Umbilical Cord between Normal Pregnancy and Preeclampsia

The umbilical cord area in the preeclampsia group was smaller (63.62 mm² [range 50.27–78.54]) than in the normal group (78.54 mm² [range 78.54–113.1]; $p < 0.001$). This is in accordance with the study by Santhi et al., conducted histomorphometry research on the umbilical cord, by dividing 15 normal pregnancies, 15 preeclampsia without severe symptoms and 15 preeclampsia with severe symptoms, respectively the area of the umbilical cord was 70,246 ± 22,710 mm² vs 58,689 ± 13,830 mm² vs 42,945 ± 18,983 mm² (Chillakuru et al., 2020). Where the area of the umbilical cord is smaller in preeclampsia than in normal pregnancy. However, this is inversely proportional to the findings by Merlin et al, that of 35 cases of preeclampsia, 28/35 (80%) had edema of the umbilical cord which caused the area of the umbilical cord to preeclampsia to be larger than in normal pregnancies (Thomas et al., 2020). A different case was also found by Sharony et al, stating that the cases of preeclampsia without BBLR (70.22 ± 18.75) were not smaller than the control group (normal pregnancy) (73.12 ± 21.87), but it looked different when compared to the preeclampsia group with BBLR (52.35 ± 15.70) the area of the umbilical cord was smaller than the control group (Sharony et al., 2016).

Based on cord blood vessels, it was found that there was no significant difference in the diameter or area of arteries A and B between the two groups ($p > 0.05$). For measures of venous diameter (2.81 ± 0.76 mm vs 2.83 mm [range 2.21–5.05]; $p = 0.377$) and venous area (6.19 mm² [range 2.05–19.53] vs 6.3 mm² [range 3.84–20.05]; $p = 0.377$) did not differ statistically. This is similar to the findings by Shanti et al, there was a cumulative similarity between arterial area A and B in the normotension and preeclampsia groups, 1,976 ± 1,141 vs 1,878 ± 0.684 (Chillakuru et al., 2020). The same was also found by Merlin et al, where the difference in the average area of the umbilical vein in normal and preeclampsia cases was not significant ($p = 0.875$), as well as the average area of the umbilical artery area in normal cases and preeclampsia ($p = 0.558$) (Thomas et al., 2020). However, contrary to the statement of Bhavina et al, they conducted the study by dividing 3 groups, the first group with normotension pregnancy, the second group with mild preeclampsia and the third group with severe preeclampsia. There was a significant difference in the area of blood vessels in the three groups, successively the area of normal arteries vs mild preeclampsia vs severe preeclampsia was 4464.45 ± 675.40 mm² vs 3249.056 ± 889.69 mm² vs 2858.477 ± 507,293 mm² (Bhavina & Radhika Krishnan, 2016).

Based on the size of the Wharton jelly area, it was found that the Wharton jelly area in the preeclampsia group was smaller (52.12 ± 9.18 mm²) than in the normal group (67.45 mm² [range 56.47–104.16]). Using the Mann Whitney test, there was a significant difference in the size of Wharton jelly's area between the group of mothers with Preeclampsia and the group of normotensive mothers ($p = <0.001$). This is in accordance with the results found by Jain Rashmi et al, Umbilical cord histomorphometry analysis showed that the average area of Wharton jelly was 35.28 mm2 in the normal group and 29.04 mm2 in the preeclampsia group, with the area of Wharton jelly significantly reduced in the preeclampsia group compared to the normal group (Jain et al., 2024). The same thing was also conveyed by Jain Ankit et al, umbilical cord histomorphometry analysis showed that the average area of Wharton jelly was 35.28 ± 8.42 mm2 in the normal group and 29.04 ± 8.09 mm2 in the preeclampsia group. The area of Wharton jelly was significantly lower in the preeclampsia group compared to the normal group (Jain et al., 2019). Gaikwad et al, also found the same thing, where the thickness of Wharton jelly in normal was 1.36 ± 0.02 mm and preeclampsia was 0.95 ± 0.04 mm (Gaikwad et al., 2022).

Analysis of the Relationship between *Wharton jelly Size* and Birth Weight of Babies from Mothers with Preeclampsia and Maternal Normosity

In the preeclampsia group, the area of Wharton's jelly did not show a significant association with infant birth weight ($p = 0.156$; $r = -0.293$). In contrast, in the normotensive group, the area of Wharton's jelly demonstrated a positive and significant correlation with infant birth weight ($p = 0.014$; $r = 0.486$), indicating that this tissue thickness may support optimal fetal growth through mechanical protection and regulation of blood flow. The correlation coefficient of 0.486 indicates a positive correlation, meaning that an increase in the area of Wharton's jelly is followed by an increase in infant birth weight among mothers with normotension, with a moderate strength of correlation ($r > 0.4–0.6$). These findings differ from those reported by Rashmi et al., who found that both infant birth weight and the area of Wharton's jelly were significantly lower in the preeclampsia group. A strong positive correlation between infant birth weight and the area of Wharton's jelly was observed in both the normal pregnancy group ($r = 0.895$, $p < 0.0001$) and the preeclampsia group ($r = 0.850$, $p < 0.0001$) (Jain et al., 2024).

According to Sharony et al., preeclampsia may or may not be associated with placental growth restriction (PGR). The umbilical cord and Wharton's jelly are not thinner in preeclampsia without PGR compared with normal pregnancies. This suggests that umbilical cord thinning is mediated by mechanisms associated with fetal growth disorders rather than abnormalities directly related to preeclampsia, which is primarily a maternal disease (Sharony et al., 2016). According to Mandana et al., placental disorders and reduced fetal blood flow due to placental dysfunction may contribute to low birth weight and preterm birth ($p < 0.001$) (Ghanaie et al., 2022). According to Marques et al., inappropriate interpretation of placental weight and birth weight relationships may occur in pregnancies with and without hypertension. Therefore, hypertension associated with impaired implantation may result in a small and dysfunctional placenta, which generally leads to low birth weight. Conversely, hypertension associated with a large placenta is unlikely to result from impaired implantation, and increased birth weight may be related to maternal factors, such as gestational diabetes mellitus or a high body mass index, as observed in this study (Marques et al., 2018).

According to Amin et al., the analysis demonstrated a strong correlation between Wharton's jelly area and birth weight ($R^2 = 0.8842$, $p < 0.001$). A positive relationship was observed between the area of Wharton's jelly and neonatal birth weight, indicating that neonatal birth weight increased consistently with increasing Wharton's jelly area (Amin et al., 2018). According to Wibowo et al., a study examining the relationship between Wharton's jelly area and birth weight among term infants from normal pregnancies reported that the mean area of Wharton's jelly in infants with normal birth weight was 56.077 ± 19.537 mm^2. The analysis demonstrated a statistically significant correlation between Wharton's jelly area and birth weight ($p = 0.041$) (Wibowo et al., 2017).

Regarding umbilical vessels, the areas of umbilical artery A and umbilical artery B were not significantly correlated with birth weight in either the preeclampsia group ($p = 0.741$; $r = 0.070$ and $p = 0.406$; $r = 0.075$, respectively) or the normotensive group ($p = 0.412$; $r = 0.172$ and $p = 0.072$; $r = -0.366$, respectively). The umbilical vein area was not correlated with birth weight in the preeclampsia group ($p = 0.720$; $r = -0.275$), but it demonstrated a significant negative correlation in the normotensive group ($p = 0.027$; $r = -0.442$). The negative correlation indicates an inverse relationship between umbilical vein area and infant birth weight, meaning that an increase in umbilical vein area was associated with a decrease in infant birth weight. The strength of the correlation between umbilical vein area and infant birth weight was moderate ($r > 0.4–0.6$). These findings differ from those reported by Soysal et al., who found no statistically significant correlation between umbilical vein diameter and other variables in correlation analysis ($p > 0.050$).

Their study concluded that there was no association between umbilical vein diameter or umbilical cord length and fetal weight in term pregnancies (Soysal et al., 2021).

According to Tutus et al., umbilical vein diameter and fetal birth weight are inversely associated in newborns and infants with low gestational age. As the diameter of the umbilical vein decreases between 20 and 24 weeks of gestation, the estimated fetal birth weight increases ($p < 0.05$). However, the underlying mechanism remains unclear (Tutus et al., 2021). According to Sangeeta et al., a statistically significant positive correlation was observed between all umbilical vascular parameters and neonatal anthropometric measurements ($p < 0.001$). This finding indicates that the area of UA2 (Umbilical Artery 2) and UV (Umbilical Vein) may serve as reliable predictors of neonatal birth weight. Furthermore, the area of the umbilical cord may represent a more accurate parameter than diameter measurement because the umbilical cord does not always exhibit a perfectly circular geometric shape (Kotrannavar et al., n.d.).

CONCLUSION

The conclusion of this study indicates that there was a significant difference in *Wharton's jelly* area between mothers with preeclampsia and those with normotensive pregnancies. The preeclampsia group demonstrated a smaller *Wharton's jelly* area compared with the normotensive group ($p < 0.001$). Furthermore, infants born to mothers with preeclampsia had significantly lower birth weights than infants born to mothers with normotensive pregnancies ($p = 0.045$). However, the association between *Wharton's jelly* area and infant birth weight varied according to pregnancy conditions. In the normotensive group, *Wharton's jelly* area showed a significant positive correlation with birth weight ($p = 0.014$; $r = 0.486$), suggesting that a greater *Wharton's jelly* area may support fetal growth through its role in maintaining umbilical blood flow and protecting umbilical vessels. Conversely, no significant correlation was found between *Wharton's jelly* area and birth weight in the preeclampsia group ($p = 0.156$; $r = -0.293$). These findings suggest that alterations in umbilical cord morphology, particularly *Wharton's jelly* characteristics, may be associated with fetal growth outcomes; however, the pathological mechanisms underlying these changes in preeclamptic pregnancies require further investigation. Future research should involve larger sample sizes and multicenter studies to improve the generalizability of findings regarding the role of *Wharton's jelly* in pregnancy outcomes. Further investigations are recommended to incorporate additional maternal, placental, and fetal factors, including the severity of preeclampsia, gestational age, maternal nutritional status, body mass index, placental function, and molecular biomarkers associated with inflammation and angiogenesis. Longitudinal studies following pregnancies from the antenatal period through neonatal outcomes are also needed to determine whether *Wharton's jelly* morphology can serve as an early predictive marker for fetal growth restriction and adverse neonatal outcomes. Moreover, integrating histomorphometric evaluation with advanced imaging techniques and molecular analyses may provide deeper insights into the potential clinical application of *Wharton's jelly* assessment as a biomarker for high-risk pregnancies, particularly those complicated by preeclampsia.

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