

Umbilical cord diameter study on microscopic tissue in gestational diabetes mellitus and its correlation to fresh tissue diameter and fetomaternal parameters



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ABSTRACT

Background: Umbilical cord is the only vital link between the mother and the fetus and is essential for maintaining the fetomaternal exchange of oxygen, nutrients, and waste products. Clinical studies have shown that umbilical cord diameter (UCD) is larger in gestational diabetes mellitus (GDM) and UCD analysis based on microscopic tissue (dry) provides more accurate information. **Aims and Objectives:** The present study was conducted to measure the UCD using microscopic tissue in GDM and normal cases and ascertain its correlation with fresh tissue (wet) diameter, fetal weight, maternal BMI, and gestational weight gain. **Materials and Methods:** The study included 111 subjects. They were divided into two groups. Group I consisted of umbilical cords obtained from non-diabetic pregnant women (n = 52) and Group II comprised umbilical cords obtained from mothers with GDM (n = 59). UCD was measured using Vernier calipers and all the other parameters were assessed through standard methods. **Results:** UCD in microscopic (P = 0.005) and fresh tissues (P = 0.0001) was significantly higher in GDM patients. Although microscopic tissue measurements tended to underestimate fresh-tissue measurements of UCD, these measurements had a positive correlation with each other in both groups. UCD also had a statistically significant positive correlation with maternal BMI and a negative correlation with gestational weight gain. **Conclusion:** UCD in GDM was statistically higher in both microscopic and fresh tissues and thus may be considered for GDM screening. The correlation of wet and dry specimens can also provide useful insights in clinical situations centered around variations in UCD.

Key words: Umbilical cord diameter; Gestational diabetes mellitus; Microscopic tissue

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INTRODUCTION

Umbilical cord is the only vital link between the mother and the fetus. It is composed of two arteries and one vein to maintain the fetomaternal exchange of oxygen, nutrients, and waste products. These blood vessels are surrounded with Wharton's jelly, a gelatinous stroma, and covered by a single layer of the amnion to provide flexibility, mobility, and strength to resist compression, whilst at the same

time, allowing the fetus to move freely. The diameter of the umbilical cord varies from 0.8 to 2 cm.¹ Gestational diabetes mellitus (GDM) is the appearance of glucose intolerance for the 1st time during pregnancy. It is the most common endocrine disorder of pregnancy which has a profound influence on the umbilical cord morphology.² GDM increases the diameter of the cord by increasing the Wharton's jelly content¹ and luminal area of vessels and edema.³ In contrast, other studies reported that there

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was no alteration in the diameter of the vessels in GDM.^{4,5} The higher content of Wharton jelly in GDM protects the umbilical vessels during uterine contractions with a cushioning effect, which permits better perfusion to the relatively large fetus during delivery.⁴ Disintegration of the endothelial lining of the umbilical arteries in GDM results in higher permeability. This may be the cause of the accumulation of fluid and plasma proteins within Wharton jelly resulting in a larger surface area and alteration in the distribution of Wharton's jelly fibers with large empty spaces within it.⁶ As the umbilical cord diameter (UCD) is larger in GDM, it is suggested that the umbilical cord dimensions may be an additional parameter to differentiate between apt for gestational age fetuses of normal pregnancies and fetuses of GDM mothers and possibly between the genetically large fetus and the macrosomic fetus of the diabetic mother.⁴ Evaluation of UCD is considered to be more accurate on microscopic tissue as calculation from volume displacement or weight methods are cumbersome processes and a single measurement of the fresh tissue would be of less value as the diameter varies in different parts of the same cord and we might measure the larger diameter of the cord that is oval in cross-section.⁵ The present study on UCD was conducted on microscopic tissue and was compared and correlated with fresh tissue diameter, fetal weight, maternal BMI, and gestational weight gain in GDM and normal cases.

Aims and objectives

The present study was conducted to measure the UCD using microscopic tissue in GDM and normal cases and ascertain its correlation with fresh tissue (wet) diameter, fetal weight, maternal BMI and gestational weight gain.

MATERIALS AND METHODS

The present study was conducted in the Department of Anatomy of P. K. Das Institute of Medical Sciences, Palakkad, Kerala. The study included 111 subjects. They were divided into two groups. Group I consisted of umbilical cords obtained from normal non-diabetic pregnant women (n=52). Group II consisted of umbilical cords obtained from mothers with GDM (n=59) diagnosed according to American Diabetic Association. The umbilical cord with the placenta was collected from the Department of Obstetrics and Gynecology within 36–40th weeks of gestation. Fetal weight, maternal height, and weight were taken from the medical records. Maternal BMI was calculated by dividing weight in kg by height in meter square. Gestational weight gain was estimated by reducing pre-gravid weight from the last trimester weight of the mother. Tagged specimens were washed clean of blood and mucus. UCD was measured using Vernier caliper (Figure 1). Portions of umbilical cords were

fixed in 10% formaldehyde, embedded in paraffin, sectioned at 5 μ m, and stained with hematoxylin and eosin as per standard placental grossing guidelines. Cord diameters were measured on the slide or all the slides using Vernier caliper (Figure 1). Diameters obtained from the normal and GDM wet and dry specimens were compared. The average mean difference between the wet and dry tissues was calculated in normal and GDM tissue. Regression analysis was done to predict the fresh (wet) tissue diameter from the dry tissue diameter. Dry tissue diameters were correlated with maternal BMI, gestational weight gain, and fetal weight in normal and GDM.

Ethical consideration

The study protocol was approved by the institutional human ethical committee of P.K. Das Institute of Medical Sciences, Kerala, India.

Data analysis

Data were analyzed using SPSS 20.0. Data were expressed as mean and standard deviation and range. Independent sample t-test was applied to observe the significance of the difference between the groups. Associations between the variables were determined by Pearson product-moment correlation. Linear regression analysis on microscopic tissue diameter measurements was done to estimate fresh-tissue measurements.

RESULTS

UCDs were significantly higher in GDM in dry and wet tissues (Table 1). Fresh-tissue measurements of UCDs were compared to UCDs obtained from microscopic tissue measurements for linear associations using the Pearson product-moment correlation. Microscopical tissue measurements of UCD were positively correlated with fresh-tissue measurements in normal and GDM but were not statistically significant. However, linear regression analysis suggested that microscopic tissue measurements tended to underestimate fresh-tissue measurements of UCD ($y=0.746x+0.487$ in normal and $y=0.468x+0.833$ in GDM), on average by 28 cm in normal pregnancies and by .32 cm in GDM pregnancies (Graphs 1 and 2). BMI ($P=0.0001$) and fetal weight ($P=0.009$) were statistically higher in GDM (Table 2). UCD had a statistically significant positive correlation with maternal BMI and a negative correlation with gestational weight gain in normal and GDM cases. ($P=0.01$) There was a statistically insignificant positive correlation between UCD and fetal weight in normal and GDM cases (Table 3).

DISCUSSION

The present study measured, compared, and correlated the UCD obtained from microscopic tissue and fresh tissue of

Table 1: Comparison of umbilical cord diameters among normal and GDM in dry and wet tissue

Diameter wet	Mean standard deviation	Minimum	Maximum	Statistical significance P-value
GDM (59)	1.303±0.1884	0.8	1.6	0.0001
Normal (52)	1.163±0.1815	0.8	1.6	
Diameter dry				
GDM (59)	0.981±0.197	0.6	1.5	0.005
Normal (52)	0.888±0.142	0.6	1.2	

GDM: Gestational diabetes mellitus

Table 2: Comparison of BMI, fetal weight, and gestational weight gain in normal and GDM

Fetomaternal parameters	Group		P-value (independent t-test)
	GDM	Normal	
BMI	23.36±3.92	20.51±3.11	0.0001
Gestational weight gain	9.19±4.52	8.40±4.00	0.338
Fetal weight	3.05±0.35	2.87±0.36	0.009

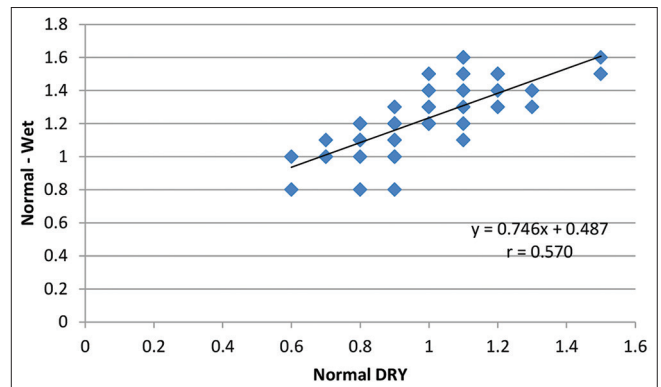
BMI: Body mass index, GDM: Gestational diabetes mellitus

Table 3: Association of umbilical cord dry diameter with maternal BMI, gestational weight gain, and fetal weight

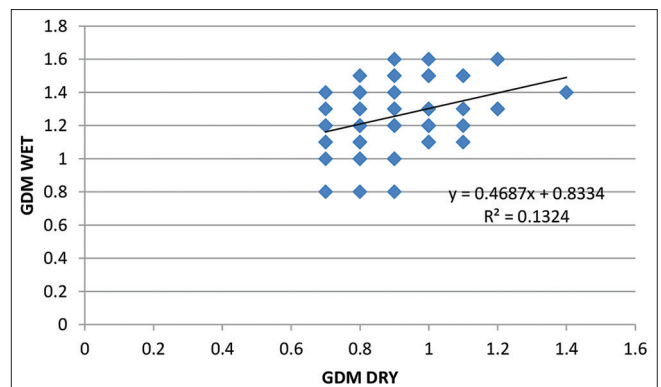
Umbilical cord dry diameter	GDM		Normal	
	Pearson correlation coefficient (r)	P-value	Pearson correlation coefficient (r)	P-value
Maternal BMI	0.997	0.01	1.000	0.01
Fetal weight	0.007	0.997	0.262	0.058
Gestational weight gain	-0.030	0.819	0.221	0.115

BMI: Body mass index, GDM: Gestational diabetes mellitus

52 normal and 59 GDM umbilical cords, and dry tissue was correlated with fetal weight, gestational weight gain, and BMI. UCD is usually encountered during routine antenatal ultrasound scanning as its alteration indicates maternal and fetal jeopardy. There is an increase in umbilical cord thickness as a function of gestational age up to 34–36 weeks of gestation, followed by a reduction of umbilical cord size.^{7,8} Assessment of umbilical cord thickness, amount of Wharton’s jelly content, and diameters of vessels, mainly umbilical vein, could be used to recognize patients who are at higher risk of intrauterine growth pattern alteration. Thin umbilical cords were found to accompany unexplained fetal death, risk of having a small for gestational age fetus at delivery, fetal distress in labor, and operative delivery whereas thick umbilical cord was observed in association with fetal hydrops, rhesus sensitization, or twin–twin transfusion. The umbilical cord thickness was found to correlate with fetal biometry, especially fetal weight and associated macrosomia.^{5,8-10} In pre-eclampsia, the UCD



Graph 1: Regression analysis among normal wet and normal dry umbilical cord diameters



Graph 2: Regression analysis among gestational diabetes mellitus (GDM) wet and GDM dry umbilical cord diameters



Figure 1: Measurement of umbilical cord diameter in fresh tissue and microscopic tissue using vernier caliper

was found to be lean with reduced Wharton’s jelly amount and a smaller umbilical vein area.⁴ Aneuploid fetuses have thick umbilical cords that are evident in the first and second

trimesters of pregnancy onwards.^{11,12} However, it was not confirmed so in some other studies.¹³ Several studies had observed an umbilical cord thickness in fetuses affected by trisomies and 21 attributed to the alteration of the extracellular matrix of the umbilical cord leading to swelling of Wharton's jelly.¹³⁻¹⁶

Umbilical cord was found significantly larger in fetuses of mothers with gestational diabetes and the main increase in cord's width was attributed to an increase in the Wharton jelly content.^{4,7,17,18} Other studies reported that there was no difference between the normal and GDM.^{19,20} In the present study, it was observed that the mean diameter of GDM umbilical cords was higher than normal in both fresh tissue and microscopic tissue measurements. Comparison between microscopic tissue, sonographic, and fresh tissue diameter in normal was done in a previous study and UCD of fresh tissue was found to be 0.56 cm less than sonographic measurements before delivery and 0.17 cm greater than UCD measured histologically.⁵ In the present study, the glass slide diameter with fresh tissue diameter in normal and GDM mothers was compared. The glass slide diameter was 0.28 cm less than fresh tissue in normal umbilical cords and 0.32 cm less in GDM umbilical cords. Heavier neonates have been reported to have larger umbilical cords.²¹ A correlation between the fetal estimated weight, Wharton jelly content, and UCD was observed in a study but none of the neonates were macrosomic.⁴ GDM cord diameter was associated with increased fetal weight in many studies.^{4-5,7} There was a statistically significant positive correlation of UCD with the maternal BMI and a negative correlation with gestational weight gain in the present study in both normal and GDM mothers. Fetal weight also had a statistically insignificant positive correlation to UCD in the normal and GDM groups.

Limitations of the study

Study results cannot be generalized as it was conducted at one center.

CONCLUSION

Mean UCD is greater in microscopic tissue ($P=0.005$) and fresh tissue ($P=0.0001$) in GDM and may be considered a screening test for GDM. The average microscopic tissue diameter is smaller by 28 cm in normal pregnancies and 0.32 cm in GDM than the fresh tissue diameter. There is a significant positive correlation between UCD of microscopic tissue and maternal BMI. Correlation of wet and dry specimens will be useful in cases where cord diameter might be an issue such as in unexplained intrauterine growth restriction or fetal demise and would increase the amount of information that can be obtained

by examining the placenta pathologically and could be of clinical significance. We recommend large-scale and multicenter studies in this area including ultrasonographic UCD studies.

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SVE- Concept, design of the study, results interpretation, review of the literature and preparing the first draft of the manuscript; **JJ-** Concept, design of the study, results interpretation, review of the literature and preparing the first draft of the manuscript; **APP-** Results interpretation, review of the literature and revision of the manuscript; **MKD-** Concept and design of the study, statistical analysis and interpretation, revision of the manuscript; **SSKG-** Concept and design of the study, statistical analysis and interpretation, revision of the manuscript.

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