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Original Article

Anatomy Section

Effects of Gestational Diabetes Mellitus on Umbilical Cord Morphology: A Comparative Study

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ABSTRACT

Introduction: Gestational Diabetes Mellitus (GDM) has great effects on umbilical cord gross morphology. Antenatal detection of altered morphology would be helpful to identify the impact of GDM on umbilical cord to reduce fetomaternal complications.

Aim: To assess and compare the morphological features of umbilical cord among gestational diabetic and normal subjects.

Materials and Methods: The study was conducted in the Department of Anatomy, PK Das Institute of Medical Sciences Palakkad, Kerala, India. The subjects included in this present study were divided into two groups. Group I consisted of normal non-diabetic pregnant women (n=52) and group II consisted of mothers with GDM (n=59). A total of 111 placentas along with the umbilical cord were collected and morphological parameters of umbilical cord such as length, diameter, circumference, coiling index, insertion, knots and number of vessels were noted. Descriptive statistical analysis was done using the statistical software SPSS version 23.0.

Results: Mean diameter (1.303±0.1884) and circumference (4.073±0.595) were found more in GDM mothers than normal (1.163±0.1815 and 3.648±0.5952) which was statistically significant (p-value 0.0001). No significant changes were observed in length, coiling index, mode of insertion and false knots among GDM and normal. The number of umbilical cord vessels was same in both the groups and true knots were absent.

Conclusion: Knowledge about the variation in the morphometric measurements of umbilical cord is important for the early detection of the maternal complications and to prevent the adverse fetal outcome.

Keywords: Circumference, Coiling index, Cord insertion, Diameter, False knot, Fetal outcome, Morphometry

INTRODUCTION

GDM is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. It is the most common medical complication of pregnancy with high maternal and fetal mortality and morbidity [1]. About 2% to 5% of the total pregnancies may be affected by diabetes mellitus. Among pregnancies complicated by diabetes mellitus, about 65% cases involve GDM, whereas 35% cases are associated with pre-existing diabetes mellitus [2]. Studies carried out in different parts of India found the prevalence of GDM ranges from 6.6% to 7.1% [3,4]. Kerala is known as the Diabetic capital of India [5]. The global increase in diabetes occurs because of population ageing and growth, increasing trends towards obesity, unhealthy diet and sedentary life style. The incidence of diabetes continues to rise and increasingly affect individuals of all ages including young adult, children and women of child bearing age during pregnancy. The increasing prevalence of type 2 diabetes in general and in younger people in particular has led to an increase in number of pregnancies with this complication [1]. Racial differences in population also influence the disease prevalence and perinatal outcome in GDM [6].

Umbilical cord, though outlives its usefulness at birth is having a paramount importance in intrauterine life as it is the only vital link between the mother and the fetus. It is composed of two arteries and one vein to maintain the feto-maternal 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 amnion to provide flexibility, mobility and strength to resist compression, while at the same time allows the fetus to move freely [7].

Umbilical cord lacks vasa vasorum and depends on the blood in the umbilical vessels and wharton's jelly for its nutrition and hence vulnerable to hypoxic injuries easily [8].

The morphology of the umbilical cord is important in understanding feto-maternal functional relationship. It can provide more clinically useful information about the placental state, as well as impeding fetal jeopardy. Diabetes exerts a heavy toll on the vascular system. Vessels of all sizes are affected from aorta down to the smallest arterioles and capillaries [9]. Maternal diabetes significantly influences the expression of genes in the umbilical cord and alters the umbilical vessel phenotype, with possible long term consequences for the neonate [10]. GDM causes rupture of endothelium of umbilical arteries, unduly dilated umbilical vein, disruption and degeneration of muscle fibers and empty spaces in the wharton's jelly [11] which would definitely have effects on umbilical cord gross morphology. GDM is an alarming threat with specific ethnicity and exacerbating factors. In the the present study we observed the morphological differences in GDM umbilical cords, an antenatal detection of which would be helpful in identifying the impact of GDM on the umbilical cord and alert the physician of the upcoming threat and to choose the correct line of treatment to reduce the fetomaternal complications.

MATERIALS AND METHODS

Study Design

This was a population based comparative study conducted in the Department of Anatomy in PK DAS Institute of Medical Sciences, Palakkad from December 2015-June 2018. According to the present criteria of the American Diabetic Association [12] mothers confirmed with pregnancy complicated by GDM and mothers with normal pregnancy following normal vaginal deliveries or caesarean section, within 36th to 40th week of gestation, were included in the study. Women having any other pathological abnormalities like pre-eclampsia, eclampsia, heart, liver, renal diseases, endocrine

disorders, malignancies and in normal pregnancies mothers having familial history of diabetes was excluded. After ethical approval from institutional ethical committee (IEC No-IEC/12-2/2015) and written consent from the patient, 59 GDM and 52 normal umbilical cords attached to placenta were procured from the operation theatre and labour room, Department of Obstetrics and Gynaecology of PK DAS Institute of Medical Sciences. The sample size was calculated based on a comparative study by Rafiqul A et al., taking morphometic measurements of cord and artery as variables and decided to be 30 GDM and 30 normal cases to make the study statistically significant [13]. All the available specimens were collected during the study period. The collected specimens were tagged and washed thoroughly to remove blood and mucus. After examining the number of vessels at the cut end of the umbilical cord from the fetal side, the number of knots was observed in the entire length of the cord.

The umbilical cord insertion was considered velamentous when it was located in the membranes, furcated when there was split in umbilical vessels and left wharton's jelly before reaching the chorionic plate surface, marginal when the distance between the cord insertion and the placental margin was less than 1 cm and central when the cord is placed at the centre and 1 cm away from the centre and the remaining were called eccentric.

Length of the cord was measured using a metallic tape from placental end to the fetal end. Length less than 30 cm is considered as short cord and more than 70 cm as long cord [7].

The Umbilical Cord Diameter (UCD) was measured using dividers placed outer-to-outer and measuring scale. Diameter less than 0.8 cm is considered thin cord and more than 2 cm as thick cord [8].

Umbilical cord circumference was calculated by the formula $\pi \times d$ (d=diameter of the cord). The coiling index was measured by dividing the number of coils by the length of the umbilical cord in cm. Coiling index below 0.1 coils/cm was considered hypocoiled and above 0.3 coils/cm was considered hypercoiled [14].

STATISTICAL ANALYSIS

Data collected were entered into Microsoft Excel spread sheet and analysed using SPSS version 23.0 software. Descriptive data tables were generated to elaborate the findings and appropriate statistical analysis was used. Descriptive statistical analysis was done which includes mean, Standard Deviation (SD), and range for various parameters. Categorical data expressed in frequencies and percentage. Continuous variables were compared using independent t-test whereas Chi-square test and Fisher's-exact test was used to compare categorical variables. The p-value <0.05 was considered as statistically significant.

RESULTS

Morphological study was done for 52 normal and 59 GDM cases having age group ranging from 18-41 years and the results were expressed in [Table/Fig-1-5]. All the cases from both the groups had normal range of diameter and circumference [7] and maximum number of cases from both the group had length and coiling index within the normal range [Table/Fig-1-3]. Mean length and coiling index was found higher in normal than GDM group but was not statistically significant. Mean umbilical cord diameter and circumference was significantly higher in GDM (p-value 0.0001) [Table/Fig-1]. In all umbilical cords two umbilical arteries and one umbilical vein were found. True knot was not present in both the groups and the number of false knot was more in GDM (13 cases vs 8 cases) though statistically not significant [Table/Fig-4]. No variation was found in umbilical cord insertion between the two groups [Table/Fig-5].

Umbilical cord	Group		p-value (Independent t-test)
	GDM	Normal	
Length Mean (cm)/SD/Range	50.305±10.0589 (24-74)	52.779±9.4384 (31-76)	0.186
Diameter Mean (cm)/SD/Range	1.303±0.1884 (0.8-1.6)	1.163±0.1815 (0.8-1.6)	*0.0001
Circumference Mean (cm)/SD/Range	4.073±0.5950 (2.5-5)	3.648±0.5952 (2.5-5)	*0.0001
Coiling index Mean (coils/cm)/SD/Range	0.2600±0.17600 (0.09-0.93)	0.2783±0.14678 (0.10-0.77)	0.987

[Table/Fig-1]: Comparison of umbilical cord length, diameter, circumference and coiling index among GDM and normal umbilical cord.
Independent t test. *: significant p-value

Umbilical cord length	Group		Total
	GDM (%)	Normal (%)	
Short cord <30 cm	1 (1.7)	0 (0)	1
Normal cord 35-70 cm	56 (94.9)	50 (96.2)	106
Long cord >70 cm	2 (3.4)	2 (3.8)	4
Total	59 (100)	52 (100)	111

[Table/Fig-2]: Classification of umbilical cord length among GDM and normal placenta.
Fischer's-exact test p-value=0.526 Not significant

Coiling index	Group		Total
	GDM (%)	Normal (%)	
Hypo coiled <0.1coils/cm	1 (1.7)	0 (0)	1
Normal coiled 0.1-0.3 coils/cm	44 (74.6)	33 (63.5)	77
Hyper coiled >0.3 coils/cm	14 (23.7)	19 (36.5)	33
Total	59 (100)	52 (100)	111

[Table/Fig-3]: Classification of coiling index among GDM and normal placenta.
Fischer's-exact test p-value=0.235. Not significant

No. of false knots	Group		Total
	GDM (%)	Normal (%)	
0	46 (78)	44 (84.6)	90
1	9 (15.3)	6 (11.5)	15
2	3 (5.1)	2 (3.8)	5
3	1 (1.7)	0 (0)	1
Total	59 (100.0)	52 (100.0)	111

[Table/Fig-4]: Comparison of false knot among GDM and normal placenta.
Fischer's-exact test p-value=0.616 Not significant

Umbilical cord insertion	Placenta		Total	Statistical significance
	GDM	Normal		
Marginal	6 (50%)	6 (50%)	12	Fischer's-exact value-8.21 p-value-0.08
Central	19 (42.2%)	26 (57.8%)	45	
Velamentous	3 (100%)	0	3	
Furcate	1 (100%)	0	1	
Eccentric	30 (60%)	20 (40%)	50	
Total	59	52	111	

[Table/Fig-5]: Comparison of umbilical cord insertion among placenta of GDM and Normal pregnancy.
Fischer's-exact test p-value=0.08. Not significant

DISCUSSION

Umbilical cord is the only lifeline between the fetus and mother. The sustenance of fetus in the intrauterine life depends upon the morphological and functional aspects of umbilical cord. In the present study we observed and compared the morphological and morphometric parameters of umbilical cord such as length, diameter, circumference, coiling index, mode of insertion, knots and number of vessels in both the GDM and normal pregnancies. Variations in the number and type of vessels present in the umbilical cord can be associated with GDM causing congenital anomalies,

intrauterine growth retardation, prematurity and perinatal morbidity [15,16]. In the present study in both GDM and normal groups we got two arteries and one vein. Three umbilical arteries were observed in a GDM case in which fusion had occurred between two through their media [13]. Single umbilical artery is found to have some association with GDM [1]. Two arteries and one vein were found in all the three groups in a study conducted on Pregnancy Induced Hypertension (PIH), pregnancy Induced Hypertension with GDM and control [17]. The diameter of umbilical cord can be larger in GDM cases compared to the normal, increase in wharton's jelly and lumen of vessels can be the reason for this [18-22]. Some studies also reported that there is no significant differences in the diameter of the umbilical cord in normal and GDM [13,17]. In the present study we found the mean diameter of GDM umbilical cords were more than the normal which was statistically significant. In accordance to the previous studies, in the present study also we found mean circumference of umbilical cords higher in GDM group which was statistically significant [21-23].

Cord length is difficult to detect through ultrasonography [24]. Factors associated with the increase in cord length can be the parity, the size of the uterine environment, increased fetal movement, male fetus, genetic background, fetal weight and women with the past history of long umbilical cord in previous pregnancies [24-26]. Decreased umbilical cord length is associated with decreased fetal movements. This can be related to the disease conditions such as down syndrome, skeletal dysplasia, central nervous system lesions that impair fetal movement, amnion bands and uterine structural malformations and multifetal gestations [24]. An excessively long or coiled cord may beat increased risk for torsion [27]. Male fetuses had longer cord length than female and vertex presentation had longer cord length than breech presentation [28]. Increase in cord length was associated with GDM in few studies [29]. A few authors couldn't find a significant relation between the GDM and cord length [30]. In our study there was no statistically significant difference in length among GDM and normal umbilical cords. Some studies shows significant correlation between the true knots of umbilical cord and GDM [29,31,32]. A few authors also reported there was no correlation between the true knots and GDM [13,21]. Folding and tortuosity of the vessels which are longer than the cord itself frequently create nodulations on the surface and are called false knots which are essentially varices [1].

In the present study, among 111 umbilical cords observed there was no case of true knot observed in normal or GDM. False knots were present more in GDM (13 cases vs 8 cases) and was not statistically significant.

Umbilical cord insertion into the placenta is varied. The distance of the umbilical cord insertion from the placental centre has been proposed as a clinically useful marker of placental insufficiency [33,34]. Central and eccentric insertions are normal and more common. Marginal velamentous and furcated are rare and associated with pathology [35]. Marginal and velamentous insertions are suggested to result from disturbances of implantation [36]. The cord insertion was found not to be significantly different between non affected pregnancies and pregnancies affected by GDM, pre-eclampsia, PIH and small for gestational age babies [14,34,37]. No significant difference was found in cord insertion in a study conducted between normal, PIH and PIH with GDM groups [16]. Marginal insertion was found in GDM group with single umbilical artery [14]. In our study there was no difference in the mode of insertion between GDM and normal group. Normal umbilical cord coiling is approximately 1 coil/5 cm of umbilical cord length or 0.20 to 0.24 coils/cm quantified via the Umbilical Coiling Index (UCI) [36]. Coiling index is probably one of the most frequently reported umbilical cord related parameters in high risk pregnancies. Pre-eclampsia and gestational diabetes have been suggested as maternal risk factors for abnormal coiling [38]. In gestational diabetes both non-coiling and hypercoiling were significantly more frequent than in normal pregnancies [39]. No significant difference was reported in umbilical cord coiling index with pre-eclampsia, PIH, GDM and small for gestational age in some studies [34].

LIMITATION

Study results cannot be generalised as it was conducted at one center. Sexual dimorphic changes in the morphology of umbilical cord and GDM with co-morbidities were not included in the study. A multicentric study on a large sample size is recommended to validate the results.

CONCLUSION

GDM increases the diameter and circumference of the umbilical cord. Maternal, fetal and placental factors can also alter the structure and morphology of umbilical cord and knowledge about these variations is important for radiologists and obstetricians for early antenatal detection and prevention of feto-maternal complications.

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