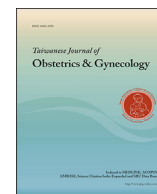


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Original Article

Antenatal umbilical coiling index in gestational diabetes mellitus and non-gestational diabetes pregnancy[☆]



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ABSTRACT

Objective: Umbilical cord abnormalities increase fetal morbidity and mortality. This study was designed to compare antenatal umbilical coiling index (aUCI) in gestational diabetes mellitus (GDM) and non-gestational diabetes mellitus (non-GDM) pregnancy, considering uncertainties about the best time to perform antenatal ultrasonography scan.

Materials and Methods: In this prospective study, 246 parturients were included, 123 with GDM and 123 with non-GDM pregnancy. Gestational diabetes was confirmed at 24–28 weeks of gestation (WG) using one-step strategy. An anatomical ultrasound survey of placenta and umbilical cord was performed at 18–23 as well as 37–41 weeks of gestational age.

Results: At 18–23 WG, the frequency distribution (10th, 90th percentiles, mean \pm SD) of the aUCI in the GDM and non-GDM groups were (0.13, 0.66, 0.32 \pm 0.19) and (0.18, 0.74, 0.4 \pm 0.31) respectively. These values were (0.12, 0.4, 0.25 \pm 0.11) in the GDM group at 37–41 WG and (0.17, 0.43, 0.29 \pm 0.11) in the non-GDM group. A significant relationship was detected between UCI value and GDM/non-GDM groups at both antenatal evaluations (18–23 WG; $P = 0.002$, 37–41WG; $P < 0.001$). A significant association at 18–23 WG was found between GDM/non-GDM groups and aUCI categorization (hypocoiling <10 th, normocoiling 10th–90th and hypercoiling >90 th) ($P = 0.001$). However, hypocoiling were significantly more frequent in GDM than non-GDM in both antenatal evaluations ($P < 0.001$, $P = 0.006$).

Conclusion: Antenatal UCI in pregnancy complicated by GDM were lower in comparison with non-GDM pregnancy. The most abnormal pattern of coiling in gestational diabetes was hypocoiling in both trimesters. In addition, 18–23 WG is the best time to perform ultrasound scan to detect aUCI and umbilical cord pattern.

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Abbreviations: AUCl, Antenatal Umbilical Coiling Index; BMI, Body Mass Index; DM, Diabetes Mellitus; FBS, Fasting Blood Sugar; GDM, Gestational Diabetes Mellitus; UCI, Umbilical Coiling Index; WG, Weeks of gestation.

[☆] **The place that study was performed:** Endocrine Research Center, Institute of Endocrinology & Metabolism and Akbarabadi hospital from Iran University of Medical Sciences (IUMS), Kamali hospital from Alborz University of Medical Sciences.

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Introduction

Life support, wellbeing and development of the fetus provides by the umbilical cord which is the major fetomaternal unit that allows gas and nutrient exchange [1].

A helix of three blood vessels (two arteries and one vein) is the major construction of the normal human umbilical cord which is protected by Wharton's jelly, amniotic fluid, helical patterns and coiling of the umbilical vessels [2–4]. Coiling is a unique and obvious feature of the human umbilical cord. The etiology, origin

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and development of this coiling is still the subject of debate [2,5] and whether it represents a genetically or an acquired phenomenon [6].

Coiling of umbilical vessels develops as early as 28 days after conception and is present in about 95% of fetuses by 9th weeks of conception [5]. Currently the standard method used to quantify the degree of umbilical vascular coiling is the umbilical coiling index [7]; which was calculated by dividing the total number of complete vascular coils by the umbilical cord length in centimeters both sonographically or immediately after delivery [7]. A frequency distribution of umbilical coiling index (UCI) was categorized by the 10th and 90th percentiles; grouping the cords as <10th percentile hypocoiled, 10th–90th normocoiled and >90th percentile hypercoiled [8]. Degani et al. have described a technique for estimating the coiling index during ultrasound examination. They found that antenatal and postnatal measurements of UCI were highly correlated; some were positively correlated while some were negatively correlated [4]. Qin et al. showed that the sensitivity of second trimester ultrasound examination for predicting hypercoiling and hypocoiling at birth were low, however, these estimates do not accurately reflect the UCI at term [9]. The umbilical abnormalities (hypocoiling, hypercoiling and non-coiling) can lead to fetal morbidity and mortality [10].

Abnormal flow, constriction or thrombosis in the umbilical cord has been postulated as the possible etiologies of adverse prenatal outcomes in the presence of the UCI abnormalities [11]. These outcomes include respiratory distress, intrauterine growth restriction, and low apgar score seen with hypocoiling and hypercoiling of the umbilical cord [12]. The increment of perinatal mortality and morbidity in gestational diabetes mellitus (GDM) parturients may have a vascular etiology [13]. Coiling could protect the umbilical cord against external forces such as tension, torsion, compression, stretching or entanglement without any effect on the cord's elasticity [11]. The most prevalent pattern of coiling in pregnancies complicated by diabetes were non-coiling and hypercoiling [4,14,15]. Gestational diabetes mellitus was found to be an important risk factor for abnormal vascular coiling of the umbilical cord [14] and has a deleterious effect on umbilical vessels and the connective tissue component of "Wharton's jelly" [16].

Considering the impact of UCI on fetal outcomes and the uncertainties about the best time to perform antenatal ultrasonography scan, the aim of this longitudinal study was to perform serial antenatal ultrasound surveys to compare the umbilical coiling index in GDM and non-GDM pregnancy.

Materials and methods

This exposure based prospective study was performed between October 10th, 2014, and August 20th, 2016. The ethics committee of Iran University of medical sciences approved the study protocol (IR.IUMS.REC.1393.24991) and the written informed consent was signed by all participants.

All 296 consecutive and unselected parturients at the 13th week of gestation were recruited into the study. Gestational age was determined (due to last menstrual period and 1st trimester ultrasound scan by crown-rump length (CRL)).

The sample size was calculated by G power software (version 11), power = 90%, α = 5%, missing rate = 20% and the mean \pm SD was used from Kurita's study [17].

Detailed history and physical examination were performed for all of the participants by an expert physician. Maternal socio-demographic, clinical, and obstetrical; ultrasound and laboratory parameters and anthropometric variables were extracted from the files and face to face interview in the first and the following prenatal visits by single trained observer. Standing height was

measured using a stadiometer (Seca gmbh& co. kg. Germany) calibrated before each measurement, and weight was measured using a calibrated digital scale (Seca gmbh& co. kg. Germany). Body mass index (BMI) defined as weight in kg/height² (meters squared) was evaluated in the first trimester prenatal visit which was the best predictor of pre-pregnancy BMI [18]. Blood pressure was measured in a standard condition (sitting position, after 5 min of resting, and ceasing smoking, drinking tea or coffee, and eating food for at least half an hour).

Gestational diabetes defined according to the American Diabetes Association (ADA) criteria at 24–28 weeks of gestation (WG) using "one-step" 75-g oral glucose tolerance test (75-g OGTT) [13]. The non-GDM group was included the parturients who were not complicated by GDM. Preexistence of risk factors were included: maternal ethnicity, age, BMI, history of complicated pregnancy, glucosuria, and family history of diabetes [19].

In the first prenatal care visit we checked the fasting blood sugar (FBS) [19], and thyroid stimulating hormone (TSH) for all parturients before 24 WG, so if we detected abnormal FBS value (92–125 mg/dL), GDM diagnosis was confirmed [20]. In these with normal results; the 75-g OGTT was performed for high risk group [19] in the first prenatal visit and for the others at 24–28 weeks of gestational age; so, if they had abnormal results they would be recruited in the GDM group and the others included in the non-GDM group. Blood glucose was measured by the Enzymatic Calorimeter method using a standard kit (EliTech kit) supplied by EliTech Group (France).

A fetal anatomical ultrasound survey (gray scale and color Doppler) of placenta and umbilical cord was performed once at 18–23 (appropriate time for evaluation of antenatal UCI (aUCI) in 2nd trimester [21]) and again at 37–41 weeks of gestational age or before delivery in preterm labor pain by one of two independent, trained, experienced, qualified and blinded ultrasonographers in each center. The Sonographic study was done by application of high resolution ultrasound equipment with color Doppler technology; Mindray DC7 unit equipped with 3.5 MHz curvilinear transducer (China).

For cord coiling assessment, the evaluation of the midsegment (free loop) of the umbilical cord by recordings of the longitudinal cord images was used [22]. The umbilical cord coiling is quantitatively assessed by the umbilical cord index (UCI).

Antenatal umbilical cord index (aUCI) was defined as reciprocal value of the distance between two consecutive umbilical coils. Umbilical cord coiling index was calculated as the number of completed coils per centimeter length of cord ($aUCI = 1/\text{distance in cm}$) [1,4,23]. The best images were obtained perpendicular to the cord. Hypocoiling and hypercoiling defined as; umbilical cords with UCI values <10th and >90th percentiles, respectively; so between 10th and 90th percentile, it was normocoiled, and where there are no coils it is described as non-coiled [7,11,14].

Single tone uncomplicated non-GDM pregnancy and pregnancy complicated by gestational diabetes, at gestational age of more than 13 weeks were included. Parturients with inadequate or incomplete antenatal, demographic, and sonographic information, multifetal pregnancy, overt diabetes, history of chronic hypertension, abortion, smoking or substance abuse, systemic disease, systemic medication use and history of any micro and macrovascular complications were excluded from our study.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (IBM SPSS statistics version 22) (IBM Corp., Armonk, NY, USA). Descriptive statistics methods were used for baseline characteristics (means \pm SD and proportions (%), or median and

interquartile range). Chi square test or Fischer exact test was used to compare discrete variables. Mann Whitney *U* test and independent sample *T*-test were used to compare two quantitative variables. Mc–Nemar test was used for testing binary variables (before, after). General linear models and logistic regression were used to adjust covariates in models. Significance was considered when *P*-value was less than 0.05.

Results

In this study, from 296 parturients, 246 with complete demographic, laboratory, and ultrasound (18–23 and 37–41 WG) data were recruited that comprises of two groups of GDM and non-GDM (123 in each group). Demographic and reproductive characteristics of parturients are summarized in Table 1.

Nulliparity was presented in 35% of total population, and significant difference was found between the two groups; 41% in non-GDM and 27% in GDM group (*P*-value = 0.004).

Preexistence of at least one risk factor; was seen in about 82% of the parturients which was more common in GDM group (94.4% in GDM vs 83.3% in non-GDM group; *P*-value = 0.001).

In comparison between two groups, GDM had higher frequency of 2 risk factors and more; than the non-GDM group (72% vs. 46%, *p*-value <0.001) (risk factors categorization in two groups 0 or 1 risk factor instead of 2 risk factors and more).

Table 2 illustrates the frequency distribution of the aUCI (10th, 90th percentiles and means ± SD) in the two groups stratified by WG. A significant relationship was detected in both trimesters between the aUCI and groups.

By adjusting the mean aUCI value of 18–23 WG, in the linear model of 37–41 WG aUCI value, we could not find a significant difference between groups and 37–41 WG aUCI value (*P*-value = 0.1); although a significant difference was found for the aUCI value of the 18–23 WG (*P*-value <0.001). It seems that this difference is due to aUCI value of the 18–23 WG that predicts aUCI at 37–41 WG.

Table 3 described the association between aUCI categorization and the two groups in two trimesters. A significant association was found between aUCI categories and groups in 18–23 WG (*P*-value = 0.001).

Hypocoiling of the umbilical vessels were significantly more frequent with gestational diabetes in 18–23/37–41 WG (*P*-value <0.001, *P*-value = 0.006 respectively).

In the GDM group, the odds ratio for hypocoiling was 3.5 (CI: 1.75–7.007) and 2.28 (CI: 1.16–4.87) at 18–23 and 37–41 WG.

By considering risk group categorization, a significant relationship was detected between the aUCI value and groups (*P*-value = 0.009).

In the stepwise linear regression model between aUCI as dependent variable and groups and baseline characteristics (maternal age, pre-pregnancy BMI, parity, history of abortion, family history of diabetes mellitus (DM), history of GDM and hypothyroidism); there were no significant relationship between aUCI and demographic/reproductive characteristics except significant relation that was confirmed between aUCI value and groups (*P*-value = 0.01).

There was not significant association between thyroid disease (hypothyroidism and hyperthyroidism) and aUCI value, and/or categorization.

Discussion

Coiling index is probably one of the most frequently reported umbilical cord related parameters in high risk pregnancies [24]. GDM as the most common metabolic complication of pregnancy is associated with maternal and fetal morbidities and it has a deleterious effect on umbilical vessels and the connective tissue components of the Wharton's jelly [16]. Furthermore, the increased perinatal mortality and morbidity associated with GDM may have a vascular etiology [16]. In this study, serial antenatal ultrasound scans were performed and midsegment of umbilical cord was examined at 18–23 and 37–41 WG. The aUCI value in non-GDM parturients was 0.4 ± 0.31 at 18–23 WG and 0.29 ± 0.11 at 37–41 WG and in GDM group was 0.32 ± 0.19 and 0.25 ± 0.11 respectively. The aUCI value was lower in GDM group than non-GDM pregnancy in both trimesters which was differed from other studies that we should determine the population selection, subgroup analysis, different range of gestational age for antenatal sonography and methodological differences as their etiologies. In another study, the UCI is on average slightly lower in normal pregnancy than in

Table 1
Demographic and reproductive characteristics of parturients.

	GDM ^a group (N = 123)	Non- GDM group (N = 123)	<i>p</i> -value
Age (yrs.) (Mean ± SD)	31.07 ± 5.19	28.01 ± 5.65	<0.001
Gravidity (Median (IQ))	2 (2,3)	2 (1,3)	0.005
Parity (Median (IQ))	1 (0,1)	1 (1,2)	0.01
History of previous abortion (No. (%))	33 (26.8%)	24 (19.5%)	0.17
History of stillbirth (No. (%))	6 (4.9%)	3 (2.4%)	0.31
History of macrosomia (No. (%))	9 (7.3%)	1 (0.8%)	0.02
History of GDM (No. (%))	19 (15.4%)	4 (3.3%)	<0.001
Family history of DM ^b (No. (%))	48 (39%)	18 (14.6%)	<0.001
Mother occupation (No. (%))			
Housewife	122 (99.2%)	118 (95.9%)	
Employee/student	0	2 (1.6%)	0.22
Others	1 (0.8%)	3 (2.4%)	
Consanguinity (No. (%))	27 (22.1%)	23 (18.7%)	0.5
Mother education No. (%))			
Lower secondary education	109 (96.5%)	108 (91.5%)	0.17
Upper secondary education	4 (3.5%)	10 (8.5%)	
Pre-pregnancy BMI ^c (Mean ± SD)	27.08 ± 3.66	25.54 ± 4.33	0.003
Thyroid disorder (No. (%))	20 (16.3%)	19 (15.4%)	0.86

Statistical analysis: data are shown as mean ± SD (Standard deviation), Median (IQ) (Interquartile) and No (%) (Number).

^a GDM: Gestational diabetes mellitus.

^b DM: Diabetes mellitus.

^c BMI: Body mass index.

Table 2
Frequency distribution of the antenatal umbilical coiling index at 18–23 and 37–41 weeks of gestation.

Gestational age	Group	aUCI ^a		Mean ± SD	P-value
		10 th percentile	90 th percentile		
18–23 WG ^b	Non-GDM ^c	0.18	0.74	0.40 ± 0.31	0.002
	GDM	0.13	0.66	0.32 ± 0.19	
37–41 WG	Non-GDM	0.17	0.43	0.29 ± 0.11	<0.001
	GDM	0.12	0.4	0.25 ± 0.11	

Statistical analysis: data are shown as mean ± SD (Standard deviation).

^a aUCI: Antenatal umbilical coiling index (coils/cm.).

^b WG: Weeks of gestation.

^c GDM: Gestational diabetes mellitus.

Table 3
Antenatal umbilical coiling index categorization stratified by gestational age.

Gestational age	Group	aUCI ^a categories				P-value
		Non-coiling	Hypo-coiling	Normo-coiling	Hyper-coiling	
18–23 WG ^b	Non-GDM ^c	11.7%	8.6%	71.2%	8.6%	0.001
	GDM	5.5%	24.7%	65.1%	4.8%	
37–41 WG	Non-GDM	0%	9.5%	81%	9.5%	0.17
	GDM	0.8%	21.7%	72.9%	4.7%	

Statistical analysis: data are shown as number (%).

^a aUCI: Antenatal umbilical coiling index.

^b WG: Weeks of gestation.

^c GDM: Gestational diabetes mellitus.

complicated pregnancy [2] but in other studies [3,24] no difference was found between these two groups.

In our study a significant relationship was detected in both trimesters between the aUCI value and GDM/non-GDM groups. But according to adjustment of the 18–23 WG value, we could not find a significant difference between GDM/non-GDM and 37–41 WG aUCI value; although a significant difference was seen for aUCI value of the 18–23 WG. It seems that this difference is due to aUCI value of the 18–23 WG that influenced the 37–41 WG value. Table 4 presented the frequency distribution parameters of the aUCI (10th, 90th percentiles and mean values) from previous studies [9,23,25–32] which were comparable with our results.

The aUCI changes between two trimesters in both groups may be due to continuous UCI changes in utero with advancing gestational age which is agreed with other studies [23,27]. So in

accordance to our finding a tendency is that the UCI decreased in the third trimester in comparison with the second trimester due to umbilical cord elongation [3,4,9,17,23,33–35]. Due to progressive change in the coiling pattern with increase in gestational age, studies performed earlier in the course of gestation (second trimester) allow more accurate evaluation of UCI [9,23,26,27,30] which was compatible with our study. In the third trimester of pregnancy, the volume of amniotic fluid is reduced, and thus the difference between the UCI and torsion is difficult to assess, and thus errors in measurement may be more frequent [9,27]. Also in our assessment, a significant association was found between aUCI categorization and non-GDM/GDM groups in 18–23 WG.

Abnormal pattern of hypocoiling of the umbilical vessels were significantly more frequent with GDM in both trimesters in our survey. Feyi-Waboso presented that GDM had significant association with the risk of abnormal coiling index [36]. Abnormal umbilical coiling patterns was significantly related to GDM in different studies such as; non-coiling [15], hypercoiling [12,15,37] and hypocoiling [14,31]. But this association was controversial as in other studies, that no significant relation was found between GDM and the aUCI value [3,24]. This controversy between previous studies and ours may related to sub group analysis in their surveys and also population selection that no specific GDM population were recruited in their projects, differences of population characteristics (age, parity, ethnicity, etc.), differences in methodologies, duration of evaluation and different trimesters for antenatal sonographic evaluations.

Adverse fetal outcomes were attributed to both hypo and hypercoiling of the umbilical cord [10], which predisposed the

Table 4
The antenatal umbilical coiling index and its categorization at different gestational age evaluations.

Author	aUCI ^a (Mean ± SD) Coils/cm	Hypocoiling 10 th > (%/No.)	Normocoiling 10 th –90 th (%)	Hypercoiling 90 th < (%/No.)	Noncoiling	Study Population	Evaluation (GA) ^b
[23]	0.4 ± 0.1	12.3% (0.21)	78.8%	8.9% (0.59)	–	Normal (236)	(18–23w ^c)
[25]	0.3 ± 0.09	8.6% (0.17)	84%	7.4% (0.41)	–	Normal (81)	(28–40w)
[9]	0.62 ± 0.2	8.8% (0.39)	80.4%	10.6% (0.9)	–	Normal (531)	(13–28w)
[26]	0.36 ± 0.07	9% (0.26)	81%	10% (0.46)	–	Normal (200)	(20–24w)
[27] ^d	–	8.9% (0.27)	80.5%	10.6% (0.64)	–	Normal (226)	(22–28w)
[28]	0.41 ± 0.3	15.6% (0.19)	75.6%	8.6% (0.54)	–	Normal (600)	(18–22w)
[29]	0.35 ± 0.08	15.5% (0.17)	–	–	–	Normal (244)	(>24w)
[30]	0.4	21% (0.24)	73%	5% (0.55)	–	Normal (223)	(>20 w)
[31]	–	12.3%	75.3%	12.3%	–	Normal (300)	(24–28w)
[32]	–	18.1%	61%	20.2%	–	GDM (149)	(28–33w)
Najafi Present study	0.32 ± 0.19	24.7% (0.13)	65.1%	4.8% (0.66)	5.5%	GDM (123)	(18–23w)
	0.25 ± 0.11	21.7% (0.12)	72.9%	4.7% (0.4)	0.8%		(37–41w)
	0.4 ± 0.31	8.6% (0.18)	71.2%	8.6% (0.74)	11.7%	Non-GDM(123)	(18–23w)
	0.29 ± 0.11	9.5% (0.17)	81%	9.5% (0.43)	0%		(37–41w)

Statistical analysis: data are shown as mean ± SD (Standard deviation) and (%) / No(number).

^a aUCI: Antenatal umbilical coiling index.

^b GA: gestational age.

^c W: Weeks.

^d Retrospective study.

vessels of the umbilical to thrombosis and/or constriction [11]. Fetal death, chromosomal or structural abnormalities, fetal heart rate disturbances, intrauterine growth retardation and interventional deliveries were more detected in hypocoiling pattern [7,8,10,11,24].

Due to prominence of the hypocoiling pattern in GDM group in our survey, an antenatal ultrasound evaluation of the aUCI in the 2nd trimester was so important to diagnose and prognosticate the adverse fetal outcomes.

The hypocoiled cords may be more susceptible to acute kinking and therefore cessation of blood flow abruptly [38], which concluded the adverse fetal outcomes.

So many investigators have reported the association between hypocoiling pattern and pregnancy complications such as: meconium staining [7,23], low apgar score at 1 min [39], low apgar score at 5 min [3,10,37], fetal distress [7,8,11,23], preterm delivery [3], aneuploidy [7], intrauterine death [3,10,11], and low birth weight [11,23,40].

So the antenatal discovery of abnormal UCI in ultrasonographic survey could lead to elective delivery of high risk fetuses, thereby preventing the fetal death rate by about one-half [11].

In our survey, an abnormal coiling in the GDM parturients, was seen in 34.9% and 27.1% during 2nd and 3rd trimesters, which was reported in 38.93% of Anusasanant's study at 28–33 WG [32]. The discrepancies of these two studies were about the GDM diagnosis strategy, different range of gestational age for antenatal sonography and different methodologies of measurements. They measured the aUCI, three times at free loop of umbilical cord and then the greatest aUCI value was reported [32]. Anusasanant's study [32] was performed without control group and their cutoffs of UCI categorization; was referred to Jo's study [27]. In Jo's study, a retrospective antenatal survey was done between 22 and 28 WG and the categorizations of abnormal aUCI were as follows: hypercoiling >0.64 coils/cm, hypocoiling <0.27coils/cm [27].

We did not discover any significant relationship between aUCI and baseline characteristics (maternal age, pre-pregnancy BMI, parity, history of abortion, family history of DM, history of GDM and hypothyroidism).

Many previous studies, had found significant correlation between UCI and maternal age and parity [2,3,9,32,35,36]. However, some studies reported strong association between increase of maternal age and abnormal UCI [31]. Extremes of maternal age were significantly associated with hypercoiling [12,15]. The age distribution in our study was differed from Anusasanant and Van Dijk's studies [2,32]. Our distribution was the same with other studies [3,15], that the subgroup analysis of age categorization [12,32], population selection (high risk population) [35], inclusion/exclusion criteria, methodological measurements and sample sizes [9,35] could be determined as differential etiologies.

Overall, the controversy in results between different studies was regarding to study design, methodological differences, methodological shortcomings, different imaging techniques, different gestational ages, different range of gestational age for antenatal sonography, small sample size, different study populations, selection bias in different studies, different health care systems, different study protocols and highly selected and/or lack of appropriate control cases.

This was a longitudinal prospective study performed at 18–23 and 37–41 WG using serial ultrasound scan to compare GDM and non-GDM pregnancy, and specifically predict the coiling pattern in these groups.

Although the part of umbilical cord that remained attached to the neonate was not assessed.

In conclusion, the aUCI values in gestational diabetes were lower in comparison with non-GDM group at both trimesters. The most abnormal pattern of coiling found in GDM was hypocoiling of the

umbilical blood vessels in 18–23 and 37–41 WG. We suggest that 18–23 WG measurement of umbilical coiling index should be part of routine prenatal ultrasonographic evaluation of women with GDM to identify UCI abnormalities.

Disclosure

- **Ethical Code:** This project was accepted by ethical committee of Iran University of Medical Sciences; ethical code: IR.IUMS.REC.1393.24991
- **Declaration of interest:** The authors (L Najafi, ME Khamseh, M Kashanian, L Younesi, A Abedini, A Ebrahim Valojerdi, Z Amoei, E Nouri Khashe Heiran, AA Keshtkar and M Malek) declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.
- **Ethical approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.
- **Informed consent:** Informed consent was obtained from all individual parturients and their spouses included in the study.

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Conflict of interest

The authors (L Najafi, ME Khamseh, M Kashanian, L Younesi, A Abedini, A Ebrahim Valojerdi, Z Amoei, E Nouri Khashe Heiran, AA Keshtkar and M Malek) declare that there is no financial and conflicts of interest that could be perceived as prejudicing the impartiality of the research reported.

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