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Relationship between placental thickness, grading, and heterogeneity in fetal growth restriction in the third trimester of pregnancy by ultrasonography and pathology tests and their relationship with estimated fetal weight and neonatal outcome

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Abstract

Introduction: The placenta is the influencing factor on the fetal weight and is as the first organ that reveals the pathological changes of pregnancy. Therefore, placental ultrasound findings influence the diagnosis of fetal growth restriction (FGR).
Objectives: This study examines the relationship between placental thickness, grading and heterogeneity during ultrasound and placental pathology in third trimester FGR fetuses and its effect on neonatal outcome.
Patients and Methods: This prospective observational study included 67 pregnant women with FGR fetuses in the third trimester of pregnancy with the mean gestational age of 34.52 ± 2.65 weeks and possible termination of pregnancy within the next seven days. The placental thickness, grading, and heterogeneity in ultrasonography were examined and compared with thickness and grading. Their effect was also considered in neonatal outcome and the results were analyzed.
Results: In this study, there is a significant relationship between the thickness of the placenta before and after birth with the weight of the placenta, weight and Apgar score, neonatal arterial pH at birth and fetal growth restriction grading in ultrasound, and neonatal outcome.
Conclusion: This study shows that ultrasonic placental findings can be effective in determining the final weight of the placenta and fetus and also the final outcome of the baby at birth. Therefore, ultrasound of the placenta should be performed along with pregnancy ultrasound.

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Introduction

A healthy child is the product of three important factors, including a healthy mother, normal genes, and proper placental implantation and growth; which highlights the role of placenta (1,2). The main function of the placenta is to provide nutrients and oxygen for the fetus to grow (3). The proper fetal growth and normal birth weight depend on the delivery of nutrients from the mother to the fetus through the placenta (4). Therefore, normal placental growth during pregnancy is essential to support a healthy fetus. Decreased placental function may negatively affect fetal growth and cause fetal growth restriction (FGR) (5,6). This relationship exists from the first trimester (7,8). FGR is a common pregnancy complication; it includes the inability of the fetus to reach the appropriate growth potential over the gestational age (9). FGR occurs in 5 to 10% of all pregnancies (10). Fetal growth disorder is associated with increasing adverse complications during pregnancy such as preeclampsia and adverse consequences in childhood and adulthood such as increased blood pressure, metabolic syndrome, insulin resistance and type 2 diabetes mellitus (11,12). In FGR, the rate of complications due to premature birth is also higher (11). Prenatal diagnosis of FGR is an important factor in preventing stillbirth (13).

Fetal growth disorder is divided into four grades based on Doppler ultrasonography indices:

Key point

In pregnancy ultrasound, placental findings can be useful in definition the prognosis of pregnancy and birth weight and also the newborn outcome. Additionally, the pathological examination of the placenta confirms this relationship.

Grade 1, which suggests mild placental insufficiency, has the following characteristics in ultrasonography; estimated fetal weight (EFW) <3rd centile and cerebroplacental ratio <5% or umbilical artery pulsatility index > 95% or middle cerebral artery pulsatility index < 5% or uterine artery pulsatility index > 95%.

Grade 2 indicates severe placental insufficiency in Doppler ultrasonography with absent end-diastolic velocity in the umbilical artery or reverse the aortic isthmus flow.

Grade 3 indicates advanced deterioration of the fetus and low-probability of fetal acidosis that exists in Doppler ultrasonography with absent end-diastolic velocity in the umbilical arteries, or ductus venosus pulsatility index >95%, along with high possibility of fetal acidosis associated with a high risk of fetal death, if there was reverse flow in ductus venosus (14).

A normal placenta with a disc-shaped appearance and rounded edges is usually seen in the anterior or posterior uterine wall that extends to the lateral walls of the uterus. The average placental thickness is usually 2 to 4 cm in which several lacunae may be seen focally (15). The placental weight during normal pregnancy is about one fifth of the weight of the fetus. Measuring the placental thickness in ultrasonography reflects the placental weight, nutritional status of the fetus, and fetal outcome (1,2). The placental thickness increases linearly with gestational age (16,17). Additionally, its thickness in millimeters is associated with the gestational age in weeks. Accurate measurements should be conducted vertically in the middle part of the placenta and near the junction of the umbilical cord and the myometrium or sub-placental vein to the amnion. The position of the placenta should be taken into account when determining its thickness. The anterior placenta is approximately 0.7 cm thinner than the posterior or fundal placenta. An anterior placenta more than 3.3 cm and a posterior placenta larger than 4 cm is thick (16). Usually, in ultrasonography, the placental thickness is checked visually, and if it is normal, no further investigation is performed, however in case of doubt, the maximum placental thickness is measured vertically at the level of the umbilical cord (18). Nevertheless, the relationship between the placental thickness and fetal weight has been inconsistent (19). Balla et al, in the sonographic examination of placental thickness in 53 Sudanese pregnant women in the second and third trimester, concluded that a thickness less than 25 mm during the third trimester is less than normal and may be a sign of growth retardation. The thickness of more than 45 mm may be a sign of maternal diabetes, blood pressure, fetal hydrops, and other disorders (20). Previously, El-Kady et al studied the relationship between placental thickness and EFW on 100 pregnant women with normal pregnancy who were at 24-28 weeks of pregnancy. There was an insignificant correlation between the actual weight of the baby and placental thickness in ultrasonography. Their study derived a new formula for EFW correction using placental thickness, which plays a promising role in predicting birth weight based on placental sonographic information (21).

Placental changes in ultrasonography are related to the fetus maturation as the placenta matures and calcifies as the pregnancy progresses. Before 37 weeks of pregnancy, significant placental calcification is rarely observed in normal fetal ultrasonography. In the week 40th or later, about 20% of placentas have extensive calcification (22).

The grading status of the placenta in ultrasonography is as follows: grade zero is observed from the end of the first trimester of pregnancy to the beginning of the second trimester of pregnancy, that is, less than 18 weeks, while the placenta is smooth and completely dense plate with uniform texture with no echogenic areas. Grade 1; between week 18 and week 29 of pregnancy, the placenta should be grade one when the chorionic plane of the placenta is a complete unbroken line and the placenta contains a few randomly distributed echogenic areas of 2 to 4 mm in size. After week 30, the grade of the placenta reaches two. In grade two, the depressions and ridges of the chorionic plate are clear, and the placenta generally has echogenic densities extending to the middle of the placenta. After the week 39 (in the last stage of placental growth), it reaches grade three. In grade three, the placenta is divided into two similar lobes, the border between these two lobes is clear, and the calcification has reached the maternal level of the placenta. The placenta looks like Swiss cheese (23,24). McKenna et al determined the importance of abnormal placental calcification in ultrasonography examination. They concluded that ultrasonography detection of placenta with grade 3 calcification at 36 weeks of gestation and earlier may help identify pregnancies at risk of subsequent gestational hypertension and FGR delivery (25). Increased placental echogenicity can be associated with placental bleeding or hypoxia (26,27). However, reduced echogenicity and jelly-like appearance can be associated with preeclampsia and FGR (28).

In some studies, the relationship between placental calcification, grading, and pregnancy outcome has been inconsistent (29). Premature calcification may reflect placental vascular insufficiency and increase the risk of adverse complications such as FGR (24). In two studies, the grade three placental calcification caused adverse pregnancy outcomes for the mother such as decompression and bleeding after delivery and adverse fetal outcomes such as low-fetal growth (30,31).

Meanwhile, Rossi et al proposed a histopathological

scoring system of placental calcification after termination of pregnancy assuming the controversial relationship between placental calcification in pathology and pregnancy outcome. They classified calcification in their pathology pattern as dusty, single and cluster. They also graded the general classification as (mild); <5 calcifications/10 fields at 10 magnifications (moderate); 5-10 calcifications/10 fields at 10 magnifications (high); >10) calcification/10 fields. They addressed the correlation between placental calcification in pathology and pregnancy outcome in 47 pregnant women and concluded that adopting a systemic approach that correlates histopathological classification grade with placental calcification grading in ultrasonography with Grannum classification and fetal/neonatal and maternal outcomes can be interesting. They found that this score of calcifications is higher in cases of maternal hypertension or FGR (29).

Objectives

Currently, placental ultrasonography characteristics are not used to determine the pregnancy outcome. Therefore, considering the importance of pregnancies with FGR and the aforementioned cases. This study compared the findings related to the outcome of the fetus, including homogeneity, grading, and placental thickness in ultrasonography with similar cases in placenta pathology. Then, it decides how far this finding helps in diagnosing FGR and determining the pregnancy outcome or carrying out treatment measures in pregnancy to change the pregnancy outcome.

Patients and Methods

Study design

This prospective observational study included 67 pregnant women based on the sample size formula of similar studies. The lowest sample size was determined as 60 patients based on the prevalence of 5% FGR during pregnancy according to the formula. The inclusion criteria were patients with FGR below the 3% percentile based on abdominal circumference or EFW, and revealed the pregnancy termination indication for maternal or fetal reasons between 28 and 37 weeks of pregnancy within seven days of sonography. The exclusion criteria were FGR polyhydramnios, fetuses with congenital anomalies, multiple pregnancies, cases that did not give birth up to one week after the ultrasonography, those who did not consent to continue the study, in case of impossibility of examining placenta after delivery, or where the pathology results did not meet the standards of the study. Sampling method was simple sequential in which patients who came for follow-up were included in the study. First a complete history, filling in the personal information of the patients, and calculating the reproductive age based on last menstrual period and Nuchal translucency ultrasonography were conducted. Then, a biometric ultrasonography was performed with a Philips A70 ultrasonography machine with 3-6 MHz prop and biparietal diameter, head circumference, abdominal circumference and femur length indices were checked. The approximate weight of the fetus was calculated, and if FGR was confirmed, the Doppler index of the fetal umbilical artery was evaluated. The average pulsatility index of the uterine artery Doppler were taken on both sides. In cases of FGR grade two and above, the Doppler status of the ductus was checked accordingly and decisions to continue the pregnancy were made based on 6th fetal health tests and Doppler ductus. The patient's bladder was half full and the uterus was at rest to check the placenta. To measure the thickness of the placenta, it was evaluated in the thickest part at the umbilical cord insertion, then the measurement was performed vertically from the chorion to the myometrium. The homogeneity and degree of placental calcification were also checked in ultrasound. Meanwhile the information was recorded in a questionnaire form. After termination of pregnancy, the placenta was separated spontaneously and sent in formalin for macroscopic and microscopic examination. Subsequently, after separating the umbilical cord and placental membranes, the placenta was weighed with a digital scale and its thickness was measured in the thickest part with a caliper, where the umbilical cord connects to the placenta after longitudinal cutting of the placenta. In the microscopic examination, the pathological calcification was examined under the single, cluster, and dust patterns. The sum of these calcifications was calculated in each placenta and recorded in the questionnaire. At birth, arterial blood gas was taken from the baby in the operating room, the 1st, 5th, and 10th minutes of the baby were recorded and the baby was weighed with a digital scale. The condition of the newborns was checked through telephone follow-up a month after birth. Placenta and fetus weights were converted into percentage based on gestational age.

Statistical analysis

The results were entered into the SPSS 26 software. Given the normality of the data distribution, they were statistically analyzed through descriptive statistics (frequency mean and standard deviation). Pearson's correlation was conducted for analyzing two quantitative variables like fetal weight in ultrasonography (EFW), pregnancy termination time, birth weight and placental weight after birth, placental weight and thickness in ultrasonography, and pathology before and after termination of pregnancy placenta thickness, Apgar and pH at birth. Independent *t* test was used for analyze quantitative and qualitative variables of two groups, such as homogeneity of placenta with EFW in ultrasound and birth weight. One-way ANOVA was applied for analyzing relation between quantitative and more than two group qualitative variables like placental thickness before and after birth with percentage of placental weight after birth. Chi-square test was used for analyzing two qualitative variables like homogeneity of the placenta and FGR of the

fetus in ultrasonography. In this study, confidence interval was considered 95% and alpha 0.05. *P* value less than 0.05 was considered as a significant value.

Results

This study examined 67 pregnant women who had FGR fetuses during pregnancy. The mean age of the mothers participating in the study was 31.4 ± 5.56 years and their mean gestational age was 34.52 ± 2.65 weeks. The lowest reported placental thickness in ultrasonography was 20 mm and the highest thickness was 67 mm with the mean of 34.46 ± 7.8 mm. The lowest EFW in the reported ultrasonography was 407 g and the highest was 2600 g with the mean of 1705 ± 605 g, which was from one to 10% based on the percentage of fetal weight. The lowest weight of the fetus at birth was 385 g and the highest weight was 2700 g with the mean of 1728 ± 618 g. The lowest placental weight in pathology examination was 100 grams and the highest weight was 570 grams with the mean of 250 ± 92.1 g, which was from one to 50% based on the percentage of placental weight. About 53.7% (36 people) had placental weight of less than 3%, 13 subjects (19.4%) had a placental weight of 3-10%, 18 (26.9%) had a placental weight of more than 10%. The lowest placental thickness in pathology was 25 mm and the highest thickness was 70 mm with the mean of 29.8 ± 9.11. The mean of the Apgar score 1st, 5th, and 20th minutes was 6.76 ± 1.65, 7.49 ± 1.76, and 7.49 ± 1.90, respectively. Around 58 subjects (86.6%) had an estimated weight of less than 3% in ultrasonography and 9 subjects (13.4%) had an abnormal weight of 3 to 10% with Doppler sonography. In testing the final calcification score of the placenta by the pathologist calculated from the sum of single, dusty, and cluster calcification, the lowest reported grade of pathological calcification was 0 and the highest was 18 with the mean of 4.22 ± 4.59 (Tables 1 and 2).

On our study, Pearson's test shows a significant and positive correlation between the EFW in sonography, birth weight, and placental weight. There is also a significant correlation between placental thickness in ultrasonography (placental thickness in ultrasonography) and its thickness in pathology (placenta thick birth). Placental weight and neonatal arterial pH at birth are shown in Table 3. There is a positive and significant correlation between Apgar 1, 5 and 10 minutes and EFW in sonography, birth weight and placental thickness in ultrasonography. Despite the significant correlation of Apgar in one and 5 minutes and placental thickness at birth, there is no significant correlation between this variable and Apgar 10. There is also a positive and significant correlation between pH at birth and all variables examined in the table.

The ANOVA test showed that there is no significant difference between placental thickness in prenatal ultrasonography and its thickness after birth with percentage of placental weight after birth (Table 4).

There was no significant relationship between placental calcification degree, FGR grading in ultrasonography,

Table 1. Mean and standard deviation of the quantitative variables

Variable	N	Mean	SD	Min	Max
Mother age (y)	67	31.10	5.56	20.00	42.00
Gestational age (wk)	67	34.54	2.66	28.00	37.00
Placental thickness ultrasonography (mm)	67	34.46	7.80	20.00	67.00
Placental thick birth (mm)	67	29.83	9.12	15.00	70.00
EFW ultrasonography (g)	67	1705.10	605.10	407.00	2600.00
Birth weight (g)	67	1728.00	618.79	385.00	2700.00
Placental weight (g)	67	250.49	92.10	100.00	570.00
Placental calcification score pathology (score)	67	4.22	4.60	0.00	18.00
Apgar 1 (score)	67	6.76	1.65	1.00	9.00
Apgar 5 (score)	67	7.49	1.76	0.00	10.00
Apgar 10 (score)	67	7.94	1.90	0.00	10.00
Calcification grade ultrasonography (score)	67	2.37	0.79	0.00	3.00

Table 2. Frequency of different levels of multilevel variables

Variable		N	Percent
Placental location (sonography)	Anterior	28	41.8
	Posterior	29	43.3
	Fundal	10	14.9
FGR grading (sonography) (score)	1	42	62.7
	2	19	28.4
	3	6	9.0
Placental calcification grading (sonography) (score)	0	1	1.5
	1	10	14.9
	2	19	28.4
	3	37	55.2
Placental weight percent after birth (percentage)	<3%	36	53.7
	3-10%	13	19.4
	>10%	18	26.9
Neonatal outcome after one month	Live	58	86.6
	Dead	9	13.4
Placental homogeneity	Homogeny	4	6.0
	Heterogenic	63	94.0
Amniotic fluid index (mm)	NL: 80-250 mm	37	55.2
	Oligohydramnios: <80 mm	30	44.8
Placental calcification score (pathology) (score)	None	22	32.8
	≤5	20	29.9
	5-10	15	22.4
	≥ 10	10	14.9
Total		67	100

Table 3. Correlation between the quantitative variables of fetal weight in ultrasonography (EFW), pregnancy termination time, birth weight and placental weight after birth, placental weight and thickness in ultrasonography, and pathology before and after termination of pregnancy (placenta thick birth, Apgar and pH at birth

Variables	Apgar 1	Apgar 5	Apgar 10	EFW (ultrasonography)	Placental thickness (ultrasonography)	Birth weight	Placental weight	Arterial pH at birth	Placenta thickness at birth
Apgar 1	1	0.86 $P=0.0001$	0.91 $P=0.0001$	0.78 $P=0.0001$	0.35 $P=0.004$	0.78 $P=0.0001$	0.58 $P=0.0001$	0.56 $P=0.0001$	0.26 $P=0.03$
Apgar 5		1	0.92 $P=0.0001$	0.81 $P=0.0001$	0.26 $P=0.03$	0.80 $P=0.0001$	0.52 $P=0.0001$	0.54 $P=0.0001$	0.17 $P=0.158$
Apgar 10			1	0.79 $P=0.0001$	0.27 $P=0.024$	0.78 $P=0.0001$	0.54 $P=0.0001$	0.53 $P=0.0001$	0.16 $P=0.178$
EFW ultrasonography				1	0.170 $P=0.156$	0.960 $P=0.0001$	0.620 $P=0.0001$	0.580 $P=0.0001$	0.070 $P=0.53$
Placental thickness (ultrasonography)					1	0.150 $P=0.212$	0.190 $P=0.112$	0.080 $P=0.513$	0.610 $P=0.0001$
Birth weight						1	0.610 $P=0.0001$	0.570 $P=0.0001$	0.080 $P=0.52$
Placental weight							1	0.400 $P=0.0001$	0.310 $P=0.01$
Arterial pH at birth								1	-0.05 $P=0.66$
Placenta thickness at birth									1

Table 4. The relationship between placental thickness ultrasonography before and after the termination of pregnancy (placental thickness at birth) and placental weight percentage

	Placental weight percentage	N	Mean	SD	F	*P* value
Placental thickness at birth (mm)	<3	36	28.55	7.92	2.124	0.128
	3-10	13	28.23	5.90		
	>10	18	33.55	12.20		
Placental thickness ultrasonography (mm)	<3	36	34.25	7.14	0.039	0.96
	3-10	13	34.46	6.48		
	>10	18	34.89	10.06		

Table 5. Correlation between Apgar score and fetal FGR grading in ultrasonography

	FGR grading ultrasonography	N	Mean	SD	F	*P* value
Apgar 1 (score)	1	67	7.48	1.11	23.749	0.0001
	2		6.05	0.91		
	3		4.00	2.76		
Apgar 5 (score)	1	67	8.31	0.95	30.749	0.0001
	2		6.69	1.06		
	3		4.33	3.08		
Apgar 10 (score)	1	67	8.78	1.12	26,039	0.0001
	2		7.10	0.74		
	3		4.67	3.78		

neonatal arterial pH at birth, neonatal outcome, fetus weight in ultrasonography, and birth weight, which checked with one-way analysis of variance tests. Moreover, there is a significant relationship between Apgar at birth and FGR grading in ultrasonography ($P \leq 0.05$; Table 5).

The one-way analysis of variance test showed, no significant relationship between the placenta location in fetal ultrasonography and any of the variables examined in this study. Likewise, chi-square test and independent *t* test showed a significant relationship between placental homogeneity and the variables of EFW in ultrasonography, birth weight, and FGR grading. However, placenta homogeneity has no significant relationship with other parameters (Tables 6 and 7).

Furthermore, no significant relationship between placental calcification scoring in pathology and any of the investigated factors in chi square and ANOVA tests was seen. Nevertheless, a significant relationship between placental calcification score and neonatal outcome in one month after birth was detected (Table 8).

Table 6. Relationship between placenta homogeneity and FGR of the fetus in ultrasonography

		FGR grade 1	FGR grade 2	FGR grade 3	Total	*P* value
Homogeneity	Homogeny	0 (0%)	4 (100%)	0 (0%)	4 (100%)	0.01
	Heterogenic	42 (66.7%)	15 (23.8%)	6 (9.5%)	63 (100%)	

Table 7. Relationship between placenta homogeneity and variables of estimated fetal weight in ultrasonography and birth weight

		N	Mean	SD	df	*P* value
EFW ultrasonography	Homogeny	4	1142.50	417.38	67	0.05
	Heterogenic	63	1740.83	600.64		
Birth weight	Homogeny	4	1159.50	349.89		0.03
	Heterogenic	63	1764.10	616.03		

Table 8. Correlation between placental calcification score in pathology and neonatal outcome in the first month after birth

		Live	Dead	Total	*P* value
Placental calcification score	Mild	35	7	42	0.05
	Moderate	15	2	17	
	Severe	8	0	8	

Discussion

The placenta is the main factor influencing fetal birth weight, and its growth abnormalities may precede fetal growth abnormalities. Since the placenta may be the first organ to reveal pathological pregnancy changes, placental characteristics plays a role in screening for pregnancy complications (21). El-Kady et al revealed an insignificant correlation between the actual weight of the baby and the placental thickness in ultrasonography (21). However, the present study found a significant relationship between the placental thickness before and after birth and the birth weight of FGR fetuses despite the smaller sample size. In this study, placental thickness in ultrasonography has no significant relationship with fetal weight in percent, which means that placental thickness should be evaluated in centimeters and fetal weight in grams to check the relationship between these two. Previously, Suseela et al studied 250 pregnant women, and related placental thickness measured at the level of umbilical cord attachment in term pregnancy to fetal birth weight. They found that the placental thickness should be used as an additional ultrasonography tool in the assessment of fetal biometrics. They showed that the placental thickness in fetuses with FGR was lower than that of fetuses with normal growth, and in cases of oligohydramnios, the accuracy of placental thickness measurement may be reduced. On the other hand, given only 20% of thin placenta in FGR cases in this study, thick placenta with FGR may be due to placental hypertrophy secondary to chronic hypoxia in the fetus (32). The amount of amniotic fluid in FGR fetuses in the present study was reduced by 44.8%, and the mean placental thickness based on gestational age was not much lower than expected based on normal gestational age, which may be explained by the hypertrophy due to chronic hypoxia. In the study by Noor et al, the placental thickness measured at the level of the umbilical cord connection between the weeks 18 and 40 can be conducted as an accurate ultrasonography index to evaluate fetal weight due to its linear correlation (33), which was consistent with our study. The difference is that this investigation was done at a higher gestational age, which confirms the present results. In the study by Ohagwu et al, on 730 Nigerian pregnant women with singleton pregnancy, a linear increase in the mean placental thickness was observed with gestational age. They also detect a positive and significant correlation between placental thickness and gestational age. Thus, placental thickness as an accurate indicator of gestational age in singleton pregnancies in Nigerian women seemed promising. However, it did not explain exactly why the in-term placental thickness in the subjects is higher than the values in other races. They finally assumed that the placenta in black people may be thicker (2). Therefore, the racial differences may also be one of the factors affecting the weight of the fetus and placental weight and thickness. In the study by Ismail et al, every 1 cm increase in Placental thickness increases fetal weight by 0.888 kg (34). Moreover, Balla et al, investigated the ultrasonography placental thickness in 53 Sudanese pregnant women in the second and third trimesters. They concluded that a thickness of less than 25 mm in the third trimester is less than normal and may indicate FGR, and a thickness of more than 45 mm is thicker than normal (20). In this report, the lowest reported thickness in ultrasonography is 20 mm and the highest thickness is 67 mm with the mean of 34.46 ± 7.8 mm in the third trimester. In pathology examination with calipers in the thickest part at the junction of the umbilical cord after longitudinal cutting of the placenta, the lowest reported thickness was 25 mm and the highest

thickness was 70 mm with the mean of 29.8 ± 9.11 mm. This result is lower than the study by Ohagwu et al, in which the mean placental thickness was examined from the weeks 28 to 41 and was 38.4 ± 7.1 mm. One reason of this result in the presents study is that in addition to FGR, the maximum age of termination of pregnancy was 37 weeks of pregnancy in fetal FGR grade 1. Moreover, the ultrasonography of placental thickness is usually greater than what is seen in the macroscopic view of the placenta after delivery. The is the drainage of blood from the placenta due to the collapse of the inter-placental spaces (35), which is the result of the present study as well. In a review of 28 studies, 1719 cases of placental syndrome were described, including 370 (21%) cases with preeclampsia or gestational hypertension, 1341 (78%) cases with FGR or small for gestational age (SGA), and 8 cases (1%) with mixed clinical expressions, which were compared with the reference group consisting of 3315 pregnant women with uncomplicated pregnancy. Placental thickness increased between the first and second trimesters in placental syndrome and was higher than uncomplicated pregnancies. Placental lakes were frequently observed in FGR and SGA pregnancies, especially in the second trimester. The association of grade 3 calcification was the most prominent point in pregnancies with placental syndrome, especially in the late second and third trimesters. Also, no grade 3 calcification was reported before the 35th week of pregnancy in the reference group. The result of the placenta appearance in pregnancies with placental syndrome shows a higher placental thickness and the presence of more lakes and calcification of the placenta compared to uncomplicated pregnancies. According to this study, standardized definitions of the (abnormal) appearance of the placenta and longitudinal research in healthy and complicated pregnancies are needed to improve personal obstetric care (36). Here, grade 2 and 3 calcifications in 56 people were observed in ultrasonography, which is more than expected for the gestational age and it is consistent with the above study. However, there was no significant relationship between the degree of placental calcification and FGR grading in ultrasonography, pH at birth, neonatal outcome, estimated weight of the fetus in ultrasonography, and the birth weight.

Recently, Paules et al observed accelerated placental aging in both clinical forms of SGA and FGR, which supports the common pathophysiology and challenges the concept of small SGA fetuses. This study also emphasizes the importance of paying attention to the placenta even in SGA cases. According to this study, the placenta does not have any morphological abnormality in the routine macroscopic and histological examination in approximately 25% of pregnancies with FGR fetuses (37). In the present study, when examining the final pathology answer, 28 people (41.9%) had normal pathology and 39 people (58.2%) had abnormal pathology, which confirms the proposed hypothesis about the pathophysiology of the above study.

Jiao Liu H et al observed that lower placental weight and its smaller surface are associated with lower birth weight and increased risk of FGR (38), which is consistent with this study. The present study also witnessed an increase in placenta grading in FGR ultrasonography.

Finally, Abramowicz and Sheiner stated that diagnostic ultrasonography has been used in clinical obstetrics for half a century. However, it seems that placenta has received less attention than the fetus or the pregnant uterus, which is somewhat unexpected considering the main functions of this organ during the entire pregnancy. Examination of the placenta plays the most important role in evaluating normal and abnormal pregnancies. The current review considered the various placental characteristics assessed by ultrasonography and the clinical significance of abnormalities of these characteristics. The numerous pathologies of the placenta can be diagnosed with routine ultrasonography. Because of the broad clinical importance and potentially severe avoidable consequences of many of these abnormalities, it is incumbent upon the physician performing obstetric sonography to examine the placenta in detail and in a targeted manner (39).

Conclusion

The final result of this study is that the parameters of the placenta, especially the thickness, homogeneity, and grading affect the perinatal outcome. The serial measurement of the placental thickness during pregnancy helps to predict the pregnancy outcome in cases of FGR, and the grading and homogeneity of the placenta in ultrasonography affects the pregnancy outcome. Abnormal placental thickness for a particular gestational age may be the first sign of intrauterine growth retardation. Fetal Doppler studies may be needed in cases of intrauterine growth restriction (IUGR) infants with very thin placentas to decide when to terminate the pregnancy. Therefore, adequate care should be taken in examining the ultrasonography of the placenta during gynecological and obstetric ultrasonography.

Limitations of the study

One of the most important limitations of our study was the follow-up of patients during delivery. Some of the samples in our study were in emergency conditions during childbirth and did not go to the hospital where the research project was conducted, or did not cooperate in sending placenta samples, so these cases were replaced with new samples.

Authors' contribution

Conceptualization: Farinaz Farahbod and Sheida Shabanian.
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Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Isfahan University of Medical Sciences approved this study (Ethical code#IR.MUI.MED.REC.1401.112). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from Sheida Shabanian fellowship (Thesis #3400891) of Maternal and fetal medicine at this university. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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