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Fetal gender-specific difference for placental volume assessed with 3D-ultrasonography

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Abstract

Objective: The aim of this study was to evaluate the effect of fetal gender in placental volume and the placental mean gray value assessed by three-dimensional (3D) ultrasonography.

Methods: This case-control prospective study consisted of 60 healthy singleton pregnancies, 29 of which were male fetuses and 31 of which were female fetuses, matched for gestational age, maternal age and parity. Placental volume and placental volumetric mean gray values were evaluated. Umbilical artery (UA) and fetal middle cerebral artery (MCA) Doppler indices were calculated.

Results: Placental volume was 296.93±108.08 and 399.12±135.08 cm^3 in male and female groups, respectively (p=0.012). Mean gray value of the placenta was 39.68±7.83 and 39.27±7.22 in male and female groups, respectively (p=0.863). UA pulsatility index (PI) was 1.03±0.21 and 1.00±0.24 in male and female groups (p=0.761) and MCA PI was 1.84±0.85 and 2.16±0.67 in male and female groups, respectively (p=0.197). Correlation analysis revealed that placental volume was not correlated with the fetal weight at the time of delivery (r=0.224, p=0.164). There was negative significant relation between placental volume and UA PI (r=-0.401, p=0.006).

Conclusion: Female fetuses have larger placental volumes which may contribute to get better results through the adverse maternal environmental conditions.

Keywords: Placental volume, 3D ultrasonography, gender-specific difference, VOCAL analysis.

Özet: Üç boyutlu ultrasonografi ile ölçülen plasenta hacminde cinsiyete bağlı değişim

Amaç: Çalışmanın amacı üç boyutlu ultrasonografi ile ölçülen plasenta hacmi ve ortalama gri değerinin fetal cinsiyete bağlı değişimini değerlendirmektir.

Yöntem: Bu olgu kontrollü prospektif çalışmaya; gebelik yaşı, anne yaşı ve parite bakımından eşleştirilmiş 29'u erkek ve 31'i dişi fetüse sahip olan toplam 60 tekil sağlıklı gebe dahil edildi. Plasenta hacmi ve plasental hacimsel ortalama gri değerleri ölçüldü. Umbilikal arter ve fetal orta serebral arter Doppler indeksleri hesaplandı.

Bulgular: Plasenta hacmi sırasıyla erkek fetüslerde 296.93±108.08 cm^3, dişi fetüslerde ise 399.12±135.08 cm^3 olarak saptandı (p=0.012). Plasentanın ortalama gri değeri sırasıyla erkek fetüslerde 39.68±7.83, dişi fetüslerde 39.27±7.22 olarak tespit edildi (p=0.863). Umbilikal arter pulsatilite indeksi erkek fetüslerde 1.03±0.21, dişi fetüslerde 1.00±0.24 olarak (p=0.761) ve orta serebral arter pulsatilite indeksi erkek fetüslerde 1.84±0.85, dişi fetüslerde 2.16±0.67 olarak saptandı (p= 0.197). Korelasyon analizinde plasental hacmin doğumdaki fetal ağırlıkla korele olmadığı gözlendi (r=0.224, p=0.164). Plasenta hacmi ve umbilikal arter arasında anlamlı ters korelasyon olduğu izlendi (r=-0.401, p=0.006).

Sonuç: Dişi fetüslerin kötü maternal çevresel koşullarda daha iyi sonuç alması, daha geniş plasenta hacimlerine sahip olmaları nedeniyle olabilir.

Anahtar sözcükler: Plasenta hacmi, 3D ultrasonografi, cinsiyete bağlı değişim, VOCAL analiz.

Introduction

New concept for analyzing the pregnancy physiology better will probably include defining fetal gender.[1] Previous studies already showed that fetal gender was related with various complications of pregnancy; the male fetuses had complications associated with defective placentation such as preeclampsia and ablatio placenta. Besides, preterm delivery and postterm pregnancy were

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more common in male fetuses whereas hyperemesis gravidarum and placental invasion anomalies were more common in female fetuses.[2–7] Moreover, detection of fetal Y-chromosomal sequences as early as 15–16 weeks of gestation has presented the opportunity to define preeclampsia before clinical syndrome occurs.[8,9] In addition, male fetuses had increased rates of cesarean section and intrapartum fetal distress.[10]

Maternal serum human chorionic gonadotropine (hCG) levels differed according to the fetal gender and were increased more prominantly in male fetuses.[11,12] Increased maternal serum hCG levels were found to be associated with lower angiogenin levels in the amniotic fluid, which suggested inadequate angiogenesis in male fetuses.[13] Steier et al. hypothesized that hCG metabolism differed according to the fetal sex and showed that hCG elimination after delivery was different in male and female newborns. During the first hour after the delivery, hCG eliminated more rapidly if the newborn was male.[14]

Few studies conducted in order to discover any association between placental histology and fetal gender. Regarding preeclamptic placentas, Naeye et al. showed that female fetuses had excessive syncytial knots as a consequence of low uteroplacental blood flow. With this finding, they suggested that male fetuses caused a greater maternal blood plasma volume expansion.[15] Regarding preterm deliveries before 32 weeks of gestation, male gender was shown to be related with chronic inflammatory placental lesions which were suggestive for the maternal immune response against the trophoblastic invasion.[16]

The aim of this study was to evaluate the effect of fetal gender in placental volume and placental mean gray value assessed by three-dimensional (3D) ultrasonograghy.

Methods

This prospective case-control study consisted of 60 pregnancies who had ultrasound examinations between January 2013 and June 2014 at our Perinatology Outpatient Clinic. Institutional Ethics Committee approved the study.

The study population consisted of 60 healthy singleton pregnancies during their third trimester and was assigned into two groups as male and female fetuses matched for the week of gestation and maternal age. The male group consisted of 29 healthy singleton pregnancies between 24 and 40 weeks of gestation (mean: 33.88±4.41 weeks). The female group included 31 singleton pregnancies aged between 24 and 40 weeks of gestation (mean: 31.71±3.77 weeks). The inclusion criteria were (1) the cases whose entire placenta could be seen and (2) the gender of the fetus defined by sonographic examination.

Gestational age was evaluated with the last menstrual period and confirmed by the early first trimester ultrasonography scans. Multiple pregnancies, women with chronic systemic disease such as diabetes, vasculitis, connective tissue disorder, hypertension/preeclampsia, hepatic or renal failure, and pregnancies with fetal chromosomal or structural anomaly were excluded from the study.

Ultrasound examinations were performed using a Voluson 730 Pro system with a RAB 3.5-MHz array probe with a combination of power Doppler and 3D/4D properties (GE Medical Systems, Milwaukee, WI, USA). All examinations were carried out via transabdominal probe by the same operator (H.G.P.). At that time, the other operator (B.A.U.) was observing the entire placenta scan and measurements independently.

2D gray scale ultrasound examinations were performed for all patients in the study group for evaluating fetal biometric measurements and placental localization according to Hadlock et al.[17] After the visualization of the entire placenta, we performed a 3D scanning with the widest scanning angle (80°). After scanning the region of interest (ROI), we used Virtual Organ

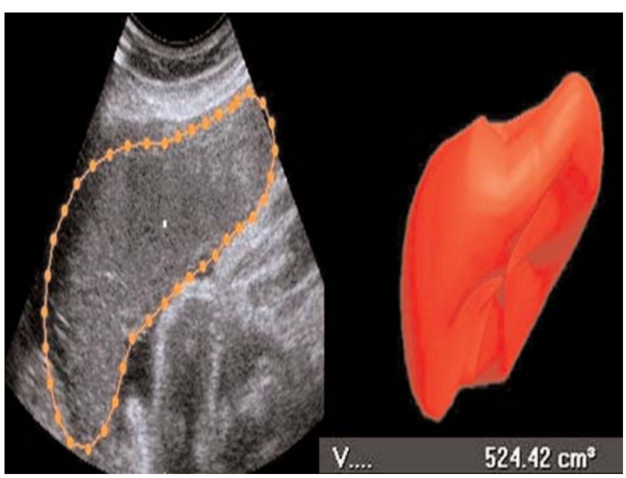

Fig. 1. Assessment of placental volume by VOCAL method.

Computer-aided Analysis (VOCAL-II) imaging software to assess the placental volume (cm^3) (VOCAL settings: manual trace, rotation angle: 30°)[18,19] (**Fig. 1**). The mean gray value represented the videodensity of the placenta as presented on the computer screen. It is expressed as a percentage with a minimum value being 0 (minimum videodensity) and maximum value being 100 (maximum videodensity)[20,21] (**Fig. 2**).

Umbilical artery (UA) Doppler measurements were obtained in the free loop.[22] Fetal mid-cerebral artery Doppler evaluation was made by obtaining a fetal axial section including fetal thalamic nuclei on the scan. Color flow mapping was used to identify the circle of Willis. The measurement was made on the proximal third of the middle cerebral artery (MCA) where it is close to its origin in the internal carotid artery.[23] All Doppler waveforms were calculated only after obtaining three consecutive waveforms.

Statistical analysis was performed by using SPSS v.20 (SPSS Inc., Chicago, IL, USA). The results were expressed in mean ± standard deviation (SD). A p value less than 0.05 was regarded as statistically significant. Student's t-test for unpaired variables was used to evaluate the group differences. Spearman's correlation analysis was conducted to investigate the relation between placental volume, mean gray values of the placenta, Doppler results and the week of gestation.

Results

Mean maternal age was 31.88±5.16 weeks and 29.14±6.21 weeks in male and female groups, respectively (p=0.162). Mean gestational age was 33.88±4.41 weeks and 31.71±3.77 weeks in male and female groups, respectively (p=0.111). Placental volume was 296.93±108.08 cm^3 and 399.12±135.08 cm^3 in male and female groups, respectively (p=0.012) (**Fig. 3**). Mean gray value of the placenta was 39.68±7.83% and 39.27±7.22% in male and female groups, respectively (p=0.863). UA pulsatility index (PI) was 1.03±0.21 and 1.00±0.24 in male and female groups (p=0.761) and MCA PI was 1.84±0.85 and 2.16±0.67 in male and female groups, respectively (p=0.197) (**Table 1**).

Correlation analysis revealed that placental volume was not correlated with the fetal weight at the time of delivery (r=0.224, p=0.164). There was negative significant relation between placental volume and UA PI (r=-0.401, p=0.006); UA resistance index (r=-0.423, p=0.002); and UA systole/diastole ratio (r=-0.370, p=0.006). Placental volume was not associated with parity, week of gestation, and mean gray value (r=0.175, p=0.111; r=0.140, p=0.135; r=-0.025, p=0.783, respectively) (**Table 2**).

Fig. 2. Assessment of the mean gray value.

Discussion

Recent studies have suggested that the placental functions differ according to the fetal gender.[1,24,25] Female and male fetuses develop through different mechanisms to get through the same adverse maternal environment in utero. Female placenta typically makes adjustments for longer survival if any adverse environmental change

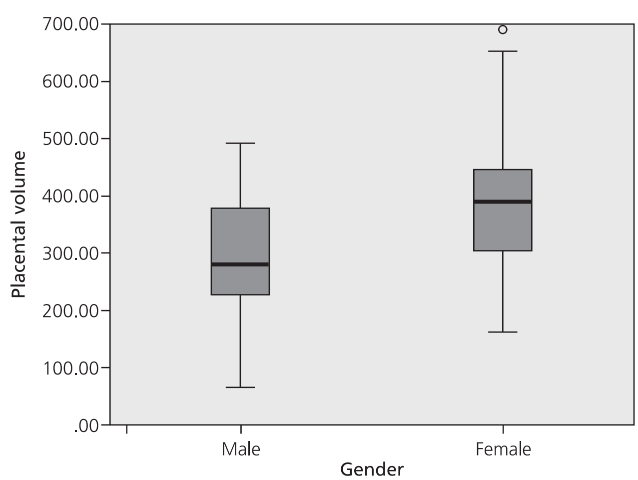

Fig. 3. Placental volume assessed by 3D ultrasonography in male and female fetuses.

Table 1. Clinical data in healthy singleton Turkish pregnancies with male and female fetuses.

	Pregnancies with male fetuses n=29	Pregnancies with female fetuses n=31	p
Maternal age (year) (mean±SD)	31.88±5.16	29.14±6.21	0.162
Parity (mean±SD)	1.06±1.03	0.71±1.10	0.330
Gestational age (week) (mean±SD)	33.88±4.41	31.71±3.77	0.111
Birth weight (gram) (mean±SD)	3160.0±709.67	3021.43±972.09	0.613
UA PI (mean±SD)	1.03±0.21	1.00±0.24	0.761
MCA PI (mean±SD)	1.84±0.85	2.16±0.67	0.197
Placental volume (cm^3) (mean±SD)	296.93±108.08	399.12±135.08	0.012*
MGV (%) (mean±SD)	39.68±7.83	39.27±7.22	0.863

*p<0.05 significant; **MCA:** middle cerebral artery, **MGV:** mean gray value, **PI:** pulsatility index, **SD:** standard deviation, **UA:** umbilical artery.

occurs.[1] Even vascularity and angiogenesis develop in a gender-different manner.[16] From that point of view, we hypothesized that placental volume and histogram may have changed regarding the fetal sex. Our study group comprised of the uncomplicated singleton pregnancies. Female placental volumes were significantly larger, although the measurements were performed approximately one week earlier in female fetuses. Our study is the first one evaluating the placental volume and mean gray value according to fetal gender.

Previous studies showed that male fetuses had poorer placentation, poorer angiogenesis and poorer adaptation mechanisms to adverse maternal conditions.[1,16] Recently, Prior et al. evaluated 388 term pregnancies and reported reduced MCA resistance and umbilical venous flow rates without any significant difference in UA PI in male fetuses[26] Similarly, we found lower MCA PI in males; however this difference has not reached to a statistically significant level. UA PI was also similar in both sexes (p=0.897). Prior et al. suggested that lower resistance in cerebral circulation in male fetuses may be a fine clue of the in-utero adaptation to the poor placentation.[26]

Placental volume may be a clue for healthy pregnancy, as recent studies showed that placental volume decreased in placental insufficiencies such as preeclampsia and intrauterine growth retardation and increased in gestational diabetes mellitus.[18,27–32] We found that male fetuses had significantly smaller placental volumes which may be a subtle suggestion for poorer placentation in males. However, our sample size –one of the limitation of our study– was relatively small and although our preliminary results show significant difference, this finding must be confirmed with larger studies. The other interesting preliminary result of our study was the indifference of volumetric mean gray value in both genders. Mean gray value describes the videodensity of the placenta; increased mean gray value means increased calcific tissue and decreased vascularity. Regarding both genders, we found no difference. The other limitation of our study was the lack of the data about the smoking status of the pregnant women participated in the study. Recent studies showed that smoking status had no effect on the placental volume.[33,34] However, it may have an effect on the placental angiogenesis and volumetric mean gray values. In the other hand, the advantage of our study was the matched groups for the gestational age, parity and maternal age.

Table 2. Correlation analysis of placental volume with the week of gestation, parity, umbilical artery PI, placental mean gray value and birth weight.

Placental volume	Week of gestation	Parity	UA PI	UA RI	UA S/D	Placental mean gray value	Birth weight
r	0.140	0.175	- 0.401	-0.423	-0.370	-0.025	0.224
p	0.135	0.111	0.006*	0.002*	0.006*	0.783	0.164

*Statistically significant; **PI:** pulsatility index, **RI:** resistance index, **S/D:** Systole/diastole, **UA:** umbilical artery.

Conclusion

In conclusion, our preliminary results, as the new findings in the literature, showed that male fetuses had significantly smaller placental volumes which may be associated with poorer placentation. This must be confirmed with larger studies.

Conflicts of Interest: No conflicts declared.

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