

# Investigation of the effects of fetal gender on umbilical artery and middle cerebral artery Doppler findings

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## Abstract

**Objective:** In this study, we aimed to investigate the effects of fetal gender on umbilical artery and middle cerebral artery Doppler measurements.

**Methods:** Umbilical artery (UA) and middle cerebral artery (MCA) Doppler ultrasonographic measurements were screened retrospectively from image and file records of 60 healthy singleton pregnant women who were on their third trimesters and referred to the Perinatology Clinic of Celal Bayar University between 2013 and 2014. Umbilical artery and MCA Doppler indexes were calculated by obtaining at least 3 consecutive waveforms. The pregnancies were evaluated in two different groups according to fetal gender (31 female fetuses and 29 male fetuses) and compared. The difference between two groups was analyzed by SPSS v.20.

**Results:** Female fetuses were identified in 31 (51.67%) out of 60 pregnancies and male fetuses were identified in 29 (48.33%) cases included in the study. Mean maternal ages of female and male fetuses were  $29.14 \pm 6.21$  and  $31.88 \pm 5.16$  ( $p=0.162$ ), and mean gestational weeks were  $31.71 \pm 3.77$  and  $33.88 \pm 4.41$  ( $p=0.111$ ), respectively. Umbilical artery PI in female and male fetuses was found as  $1.00 \pm 0.24$  and  $1.03 \pm 0.21$ , respectively ( $p=0.761$ ). Middle artery PI in female and male fetuses was found as  $2.16 \pm 0.67$  and  $1.84 \pm 0.85$ , respectively ( $p=0.197$ ). Cerebral-umbilical rate was calculated as MCA PI/UA PI. Although cerebral-placental rate was not statistically significant, it was higher in female fetuses; while it was  $1.86 \pm 0.92$  in male fetuses, it was  $2.23 \pm 0.78$  in female fetuses ( $p=0.172$ ).

**Conclusion:** Today, the new approach is not to ignore the gender of baby during intrauterine period. The decrease in MCA resistance of male fetuses should be evaluated in greater studies.

**Keywords:** Fetal gender, Doppler, middle cerebral artery (MCA), umbilical artery (UA).

## Özet: Fetal cinsiyetin umbilikal arter ve orta serebral arter Doppler bulgularına etkisinin araştırılması

**Amaç:** Bu çalışmada fetal cinsiyetin, umbilikal arter ve orta serebral arter Doppler ölçümlerine etkisini araştırmayı amaçladık.

**Yöntem:** 2013-2014 yıllarında Celal Bayar Üniversitesi Perinatoloji Polikliniğine başvuran üçüncü trimesterde olan 60 sağlıklı tekil gebelikte yapılmış olan umbilikal arter (UA) ve orta serebral arter (MCA) Doppler ultrasonografik ölçümleri retrospektif olarak görüntü ve dosya kayıtlarından tarandı. Umbilikal arter ve MCA Doppler endeksleri en az ardışık 3 dalga formu elde edilerek hesaplandı. Gebelikler fetal cinsiyete göre iki ayrı grupta değerlendirildi (kız fetüsler 31 ve erkek fetüsler 29 olgu) ve karşılaştırıldı. Her iki grup arasındaki fark SPSS v.20 ile değerlendirildi.

**Bulgular:** Çalışmaya dahil edilen 60 gebeliğin 31 tanesinde kız fetüs (%51.67) ve 29 tanesinde erkek fetüs (%48.33) tespit edildi. Kız ve erkek fetüslerde sırası ile ortalama maternal yaş  $29.14 \pm 6.21$  ve  $31.88 \pm 5.16$  ( $p=0.162$ ), ortalama gestasyonel hafta  $31.71 \pm 3.77$  ve  $33.88 \pm 4.41$  ( $p=0.111$ ) olarak tespit edildi. Umbilikal arter PI kız ve erkek fetüslerde sırası ile  $1.00 \pm 0.24$  ve  $1.03 \pm 0.21$  olarak tespit edildi ( $p=0.761$ ). Orta serebral arter PI kız ve erkek fetüslerde sırası ile  $2.16 \pm 0.67$  ve  $1.84 \pm 0.85$  olarak tespit edildi ( $p=0.197$ ). Serebro-umbilikal oran MCA PI/UA PI olarak hesaplandı. Serebro-plasental oran, istatistiksel olarak anlamlı olmamakla birlikte kız fetüslerde daha yüksek olarak bulundu; erkek fetüslerde ortalama  $1.86 \pm 0.92$  iken kız fetüslerde ortalama  $2.23 \pm 0.78$  idi ( $p=0.172$ ).

**Sonuç:** Günümüzdeki yeni yaklaşım intrauterin dönemde bebeğin cinsiyetinin göz ardı edilmemesi yönündedir. Erkek fetüslerde MCA rezistansında azalma daha büyük çalışmalarda değerlendirilmelidir.

**Anahtar sözcükler:** Fetal cinsiyet, Doppler, orta serebral arter (MCA), umbilikal arter (UA).

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## Introduction

Ultrasonographic examination is one of the most important tools of modern obstetric practice. In particular, Doppler ultrasonography provides valuable data about fetal circulation and fetal hemodynamic condition.<sup>[1]</sup> The vessels most frequently used for the evaluation of the fetal well-being are umbilical artery (UA), middle cerebral artery (MCA), and ductus venosus (DV).<sup>[2]</sup> In case of placental failure and associated fetal stress, the increases in umbilical artery resistance indexes are the leading hemodynamic changes in fetus.<sup>[3]</sup> Following these changes, MCA resistance indexes decrease as a result of cerebral redistribution, which helps to maintain blood flow towards fetal brain by this adaptation mechanism.<sup>[4]</sup>

In the studies of Askling et al. and James, the increases of placental dysfunction in male fetuses and of associated gestational complications such as preeclampsia and ablatio placentae were shown.<sup>[5,6]</sup> Also, an increase in preterm labor and postterm pregnancy frequency was found in male fetuses.<sup>[7-10]</sup> Intrapartum fetal distress and increased cesarean rates are also observed more frequently in male fetuses.<sup>[11]</sup> Besides, hyperemesis gravidarum and placental invasion anomalies are more frequent in female fetuses.<sup>[6]</sup>

Based on fetal gender being effective on placentation, we considered that fetal gender might cause a change in Doppler indexes that we use for placental perfusion evaluation, and we aimed in this study to investigate the effect of fetal gender on umbilical artery and fetal middle cerebral artery flow measurements.

## Methods

Sixty healthy singleton pregnant women who were on their third trimesters between 28 and 36 weeks of gestation and had their Doppler ultrasound examination in the perinatology clinic of our hospital between January 2013 and June 2014 were included in the study. The study group was separated into two groups by pairing according to week of gestation and maternal age, and fetuses being male and female. While 29 cases were identified as male fetuses, 31 cases were female fetuses. Approval of Local Ethics Committee was obtained for the study planned retrospectively.

Week of gestation was calculated according to the last menstrual period (LMP) and it was confirmed by

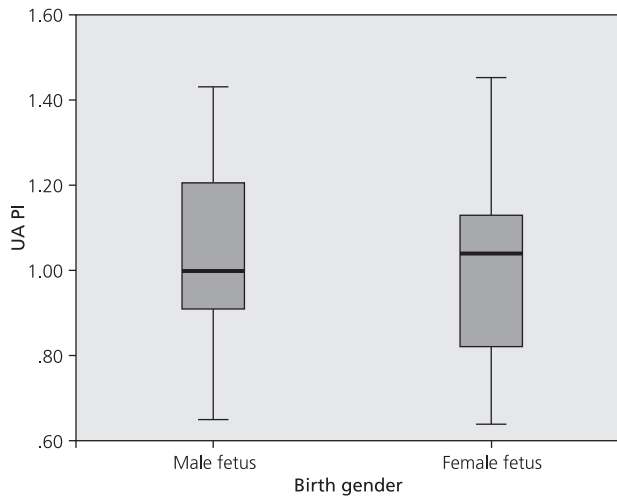
first trimester ultrasound findings. Multiple pregnancies, pregnant women with chronic systemic diseases (such as diabetes, liver and kidney diseases, connective tissue disease etc.) and pregnancies with preeclampsia and intrauterine growth retardation were excluded from the study. Also, the pregnancies found to have fetal chromosomal or structural anomalies were excluded from the study.

Ultrasound measurements were done by using Voluson 730, RAB 3.5-MHz probe (GE Medical Systems, Milwaukee, WI, USA). All measurements were done by a single operator (H.G.P.). Umbilical artery Doppler measurements were done through free region.<sup>[12,13]</sup> MCA Doppler measurement was done on the axial section where thalamic nuclei are seen on the display. Willis polygon was distinguished by color flow. The measurements were done through the proximal 1/3 part close to the internal carotid artery with origin. Doppler indexes were calculated by obtaining 3 consecutive waveforms. Amniotic fluid index (AFI) was considered as the total of amniotic fluid depths measured on 4 quadrants.

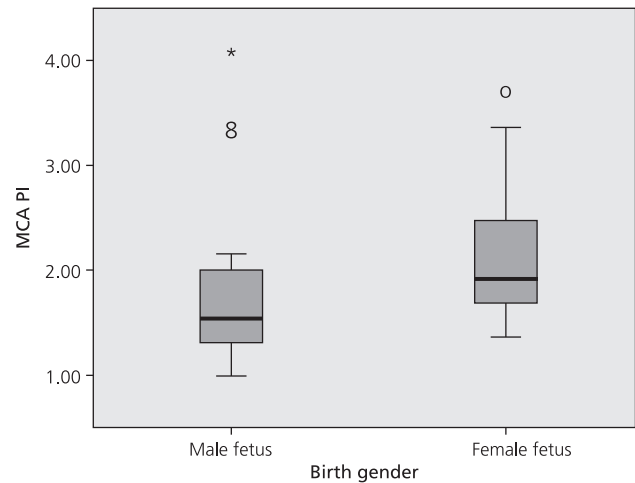
The statistical analysis was done by SPSS v.20 (SPSS Inc., Chicago, IL, USA). The results were provided as mean±standard deviation (SD). The p value less than 0.05 was considered as statistically significant. The difference between the groups was calculated by using t-test.

## Results

Female fetuses were identified in 31 (51.67%) out of 60 pregnancies and male fetuses were identified in 29 (48.33%) cases included in the study. Mean maternal ages of female and male fetuses were 29.14±6.21 and 31.88±5.16 (p=0.162), and mean gestational weeks were 31.71±3.77 and 33.88±4.41 (p=0.111), respectively. Umbilical artery PI in female and male fetuses was found as 1.00±0.24 and 1.03±0.21, respectively (p=0.761) (**Fig. 1**). Middle umbilical artery PI in female and male fetuses was found as 2.16±0.67 and 1.84±0.85, respectively (p=0.197) (**Fig. 2**). Cerebral-placental rate was calculated as MCA PI/UA PI. Although cerebral-placental rate was not statistically significant, it was higher in female fetuses; while it was 1.86±0.92 in male fetuses, it was 2.23±0.78 in female fetuses (p=0.172). The clinical data about the study group are shown in the **Table 1**. No sig-



**Fig. 1.** UA PI values in female and male fetuses.



**Fig. 2.** MCA PI values in female and male fetuses.

nificant relation was found between UA PI & MCA PI and maternal age & parity (**Table 2**). AFI was found as  $14.86 \pm 4.28$  in male fetuses and  $13.99 \pm 5.42$  in female fetuses ( $p=0.594$ ). There was no significant relationship between AFI and estimated fetal weight ( $r=0.131$ ;  $p=0.368$ ) and the week of gestation ( $r=0.008$ ;  $p=0.958$ ).

## Discussion

In our study, although we did not observe any statistically significant level in male fetuses, we identified decreased MCA resistance and slightly increased umbilical artery resistance. Although different placentation processes and implantation and angiogenesis pathways are defined depending on the fetal gender, Doppler difference associated with fetal gender in terms of evaluat-

ing placental perfusion has been analyzed only in one study so far.<sup>[14]</sup> A total of 388 term pregnant women were included in this study carried out by Prior et al., and 212 (54.6%) male and 176 (45.4%) female fetuses were identified in these pregnancies. In this study, no difference was observed between fetal genders in terms of UA PI. MCA PI was higher among female fetuses (mean female fetus value: 1.42; mean male fetus value: 1.34) ( $p=0.004$ ). MCA PSV (peak systolic velocity) was higher in female fetuses ( $p<0.001$ ). Mean cerebral-umbilical rate was 1.74 in male fetuses and 1.81 in female fetuses ( $p=0.10$ ). Umbilical venous velocity was higher in female fetuses ( $p=0.009$ ).

It was shown in previous studies that male fetuses are more associated with placental insufficiency and therefore the gestational complications related with placenta-

**Table 1.** Clinical characteristics of the pregnant women included in the study.

	Pregnancies with male fetuses n=29	Pregnancies with female fetuses n=31	p
Maternal age (mean $\pm$ SD)	31.88 $\pm$ 5.16	29.14 $\pm$ 6.21	0.162
Parity (mean $\pm$ SD)	1.06 $\pm$ 1.03	0.71 $\pm$ 1.10	0.330
Week of gestation (mean $\pm$ SD)	33.88 $\pm$ 4.41	31.71 $\pm$ 3.77	0.111
Birth weight (g) (mean $\pm$ SD)	3160.0 $\pm$ 709.67	3021.43 $\pm$ 972.09	0.613
UA PI (mean $\pm$ SD)	1.03 $\pm$ 0.21	1.00 $\pm$ 0.24	0.761
MCA PI (mean $\pm$ SD)	1.84 $\pm$ 0.85	2.16 $\pm$ 0.67	0.197
Cerebral-umbilical rate (mean $\pm$ SD)	1.86 $\pm$ 0.92	2.23 $\pm$ 0.78	0.172
AFI (cm) (mean $\pm$ SD)	14.86 $\pm$ 4.28	13.99 $\pm$ 5.42	0.594

**Table 2.** Relationship between UA & MCA PI and maternal age and parity\*.

		Maternal age	Parity
UA PI	r	0.014	-0.261
	p	0.922	0.089
MCA PI	r	0.101	0.041
	p	0.489	0.779

\*Spearman's correlation analysis; r=Spearman's correlation coefficient

tion failure (such as miscarriage, intrauterine loss, preeclampsia, IUGR etc.) are observed more frequently in male fetuses.<sup>[5,6]</sup> In a study evaluating pregnancies with loss of end diastolic flow, it was shown that 63.2% of the cases were male fetuses, and 83% of the pregnancies with reverse end diastolic flow were male fetuses.<sup>[15]</sup> Prior et al. reported that decreased resistance in MCA flow even in the male fetuses considered to have uterine artery flow and umbilical artery flow within normal ranges and to have fetal growth compatible with the week of gestation and normal placental functions compared to female fetuses depends on a physiological adaptation to the various levels of placentation in male fetuses.<sup>[14]</sup> Also, Ghidini and Salafia, and Clifton showed in their studies that the progress of angiogenesis is weaker in male fetuses and it is more difficult for male fetuses to adapt poor maternal environmental conditions.<sup>[16,17]</sup> By the change of maternal conditions during intrauterine period, the responses of male and female fetuses towards these poor conditions and the steroidogenesis pathways in this process and protein and gene expressions vary.<sup>[17]</sup> Male fetuses may adapt better to the poor intrauterine micro-environment molecularly and metabolically.<sup>[17]</sup> So, male fetus differ molecularly even in the implantation and placentation phases of pregnancy. Presence of decreased resistance in MCA flow even in male fetuses displaying normal clinical development may show that male fetuses have a physiological adaptation to the differences in placentation.

Cerebral-umbilical rate is the most reliable measurement showing brain sparing effect in babies with IUGR.<sup>[18]</sup> In our study, we did not find any difference between female and male fetuses in terms of cerebral-umbilical rate. However, we also did not expect a significant difference in terms of cerebral redistribution since our study group consisted of healthy pregnant women at their third trimesters. In the study of Yücel et al. where

Doppler findings of term pregnancies were compared according to fetus genders, there was no significant difference between female and male fetuses in terms of UA and MCA pulsatility indexes.<sup>[19]</sup>

In our study, we did not observe any significant difference in female and male fetuses in terms of AFI. In their study, Perni et al. reported a positive correlation between AFI and fetal weight in female fetuses before 38 weeks of gestation.<sup>[20]</sup> In our study, there was no association between AFI and estimated fetal weight and the week of gestation.

The weakest aspect of our study was the population size. Our study was limited with 60 patients since we planned the study retrospectively and excluded the babies with chronic disease, placental insufficiency findings or fetal anomaly from the study. By this size, the power of the study was 0.6 ( $\alpha$ -error= 0.05; d=0.5). The advantage of our study was that it was paired by the maternal age, parity and the week of gestation when the cases were separated as female and male fetuses. Also, measuring values by a single operator minimized the inter-observer difference.

## Conclusion

Consequently, placentation perfusion may vary depending on the fetal gender. Our preliminary results we provided here should be confirmed by further comprehensive studies.

**Conflicts of Interest:** No conflicts declared.

## References

1. Alfirevic Z, Stampalija T, Gyte GML. Fetal and umbilical Doppler ultrasound in high-risk pregnancies. Cochrane Database Syst Rev 2010;(1):CD007529.
2. Mari G, Abuhamad A, Cosmi E, Segata M, Altaye M, Akiyama M. Middle cerebral artery peak systolic velocity: technique and variability. J Ultrasound Med 2005;24: 425–30.
3. Piazzze J, Padula F, Cerekja A, Cosmi EV, Anceschi MM. Prognostic value of umbilical-middle cerebral artery pulsatility index ratio in fetuses with growth restriction. Int J Gynaecol Obstet 2005;91:233–7.
4. Vyas S, Nicolaides KH, Bower S, Campbell S. Middle cerebral artery flow velocity waveforms in fetal hypoxaemia. Br J Obstet Gynaecol 1990;97:797–803.
5. Askling J, Erlandsson G, Kaijser M, Akre O, Ekblom A. Sickness in pregnancy and sex of child. Lancet 1999;354: 2053.

6. James WH. Sex ratios of offspring and the causes of placental pathology. *Hum Reprod* 1995;10:1403–6.
7. James WH. Why are boys more likely to be preterm than girls? Plus other related conundrums in human reproduction. *Hum Reprod* 2000;15:2108–11.
8. McGregor JA, Leff M, Orleans M, Baron A. Fetal gender differences in preterm birth: findings in a North American cohort. *Am J Perinatol* 1992;9:43–8.
9. Cooperstock M, Campbell J. Excess males in preterm birth: interactions with gestational age, race and multiple birth. *Obstet Gynecol* 1996;88:189–93.
10. Divon MY, Ferber A, Nisell H, Westgren M. Male gender predisposes to prolongation of pregnancy. *Am J Obstet Gynecol* 2002;187:1081–3.
11. Bekedam DJ, Engelsbel S, Mol BWJ, Buitendijk SE, van der Pal-de Bruin KM. Male predominance in fetal distress during labor. *Am J Obstet Gynecol* 2002;187:1605–7.
12. Burrell SJ, Kingdom JC. The use of umbilical artery Doppler ultrasonography in modern obstetrics. *Curr Opin Obstet Gynecol* 1997;9:370–4.
13. ISUOG Practice Guidelines. Use of Doppler ultrasonography in obstetrics. *Ultrasound Obstet Gynecol* 2013;41: 233–9.
14. Prior T, Wild M, Mullins E, Bennett P, Kumar S. Sex specific differences in fetal mid cerebral artery and umbilical venous doppler. *PLoS One* 2013;8(2):e56933.
15. Edwards A, Megens A, Peek M, Wallace EM. Sexual origins of placental dysfunction. *Lancet* 2000; 355:203–4.
16. Ghidini A, Salafia CM. Gender differences of placental dysfunction in severe prematurity. *BJOG* 2005;112:140–4.
17. Clifton VL. Review: Sex and the human placenta: mediating differential strategies of fetal growth and survival. *Placenta* 2010;31 Suppl:S33–9.
18. Gramellini D, Folli MC, Raboni S, Vadora E, Merialdi A. Cerebral-umbilical Doppler ratio as a predictor of adverse perinatal outcome. *Obstet Gynecol* 1992;79:416–20.
19. Yücel A, Yılmaz M, Acar M, Değirmenci B, Köse S, Haktanır A, Fenkçi V, Cevrioglu S. Termde normal gebelerde, Doppler indeksleri ve non-stres test değerlerinin fetus cinsiyetine göre karşılaştırılması. *Kocatepe Tıp Dergisi* 2005;6: 19–24.
20. Perni SC, Predanic M, Cho JE, Kalish RB, Chasen ST. Association of amniotic fluid index with estimated fetal weight. *J Ultrasound Med* 2004;23:1449–52.