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Impact of fetal sex combinations on maternal, pregnancy, and neonatal outcomes in dichorionic twin pregnancies

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ABSTRACT

Aims: The aim of this study was to investigate the impact of concordance and discordance in fetal sex on maternal, pregnancy, and neonatal outcomes in dichorionic twin pregnancies.

Methods: This retrospective cohort analysis includes DCDA twin pregnancies delivered at Ankara Etlik City Hospital from January 2023 to December 2024. Pregnancies were categorized into three distinct groups according to the combinations of fetal gender: male-male (group 1), female-female (group 2), and male-female (group 3). Maternal demographic, pregnancy, and neonatal outcome data were compared. Composite adverse perinatal outcome (CAPO) was defined as severe neonatal complications. Chi-square, one-way ANOVA, Kruskal-Wallis, and post-hoc analyses were applied with confounder adjustment.

Results: Male-male pregnancies were also characterized by significantly increased maternal age, BMI, parity, and diabetic disease rates compared with female-female pregnancies ($p<0.05$). Neonatal outcomes indicated a considerable increase in biparietal diameter, head circumference, and abdominal circumference in group 1 and group 3 pregnancies compared with group 2 pregnancies ($p<0.01$). Additionally, male babies from discordant pregnancies weighed considerably more at birth compared to children born from concordant pregnancies ($p=0.04$); no notable differences were seen in female infants ($p=0.84$). Gestational age at birth, preterm labor percentages, and neonatal intensive care unit admission were comparable among groups ($p>0.05$). CAPO rates did not vary between groups significantly ($p=0.396$).

Conclusion: Fetal sex combinations impact neonatal and maternal outcomes of dichorionic twin gestations in varying patterns that differ in male-male versus male-female pregnancies. Greater multicenter numbers are necessary to validate the observations and investigate more fully their consequences for maximally optimizing antenatal treatment and further enhancing perinatal outcome for twin pregnancy.

Keywords: Fetal sex combinations, dichorionic twin pregnancies, maternal and neonatal outcomes

INTRODUCTION

Dichorionic twin pregnancies consist of fraternal twins in which each fetus has its own placenta and account for approximately 70% of all twin pregnancies. This type of pregnancy has a lower risk of complications compared to monochorionic pregnancies.[1] In these pregnancies, the proportion of boy/boy or girl/girl combinations varies between approximately 30-35%, with the boy/girl combination being the most common group with approximately 33-36%.[2]

Twin pregnancies offer a unique model for understanding the consequences of fetal gender and other factors on pregnancy and neonatal outcomes, as multiple fetuses share the same environment. Among these factors, fetal sex has been shown to influence not only pregnancy complications but also neonatal outcomes, revealing sex-based physiological differences.[3] Studies have shown that male fetuses are correlated with an elevated chance of preterm birth, gestational diabetes and macrosomia, whereas female fetuses are associated with preeclampsia and reduced birth weight. These results are often ascribed to hormonal and genetic differences between male and female fetuses, such as androgen exposure and alterations in placental function.[4,5] In twin pregnancies, these sex-related differences may be further accentuated by the presence of a co-fetus. Studies show that male/male twin pregnancies are linked to reduced gestation lengths and increased likelihood of adverse neonatal outcomes such as respiratory distress and low birth weight. In contrast, girl/girl twin pregnancies have shown more favorable outcomes, such as lower rates of neonatal morbidity. Interestingly, mixed-sex pairs (boy/girl twins) may provide a protective effect; it has been suggested that male fetuses may benefit from the presence of a female co-fetus.[6]

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Despite these findings, the interaction among fetal gender combinations and pregnancy outcomes in DCDA twin pregnancies remains understudied. Existing literature has often focused on isolated neonatal parameters or maternal outcomes, leaving a gap in comprehensive assessments of the impact of sex combinations on both pregnancy and neonatal outcomes. To address this gap, this study proposes to assess the outcomes of three distinct fetal gender combinations on maternal, pregnancy and neonatal outcomes in dichorionic-diamniotic twin pregnancies.

METHODS

Approval from the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee was secured for the study protocol (Date: 25.12.2024, Decision No: AEŞH-BADEK-2024-1200), and the study was conducted in keeping with the principals of the Declaration of Helsinki. This retrospective cohort study included DCDA twin pregnancies between January 2023 and December 2024 at the Perinatology Clinic of Ankara Etlik City Hospital. The study evaluated the effect of fetal gender combinations on pregnancy and neonatal outcomes.

The research population comprised all twin pregnancies confirmed to be DCDA by first trimester ultrasound and delivered at or after 24 weeks of gestation. Participants were divided into three groups according to fetal gender combinations: male/male (group1), female/female (group 2), and male/female (group 3). Inclusion criteria were live birth of both fetuses and complete medical records. Exclusion criteria were monochorionic or monoamniotic twins, fetal anomalies, intrauterine infections, twin-to-twin transfusion syndrome (TTTS), stillbirths or pregnancies resulting in neonatal death within the first 24 hours after birth. Cases with incomplete medical records were also excluded.

Data were collected retrospectively from patient records and included maternal demographic information, obstetric history and pregnancy outcomes. Maternal data included maternal age, parity, gestational age at delivery and mode of delivery. Neonatal outcomes included birth weight, Apgar scores at 1 and 5 minutes, neonatal intensive care unit (NICU) admission rates, and combined analysis of adverse neonatal outcomes such as respiratory distress syndrome, sepsis, hypoglycemia and intraventricular hemorrhage.

The primary outcomes were differences in neonatal outcomes, including birth weight, NICU admission rates, and Apgar scores, across the three fetal sex combinations. Secondary outcomes were maternal outcomes. Statistical analyses were performed using SPSS version 25.0. Categorical variables were analyzed using the Chi-square test or Fisher's exact test, while continuous variables were evaluated with one-way ANOVA or the Kruskal-Wallis test, depending on the data distribution. Post-hoc analyses with Bonferroni correction were conducted to identify significant intergroup differences. Logistic regression models were used to adjust for confounding variables, including maternal age, parity, and gestational age at delivery. Statistical significance was defined as $p<0.05$.

For further analysis, fetal sex combinations were categorized as concordant (both fetuses of the same sex: male-male or female-female) and discordant (one male and one female). Concordant pregnancies included group 1 (male-male) and group 2 (female-female), while discordant pregnancies corresponded to group 3 (male-female).

In this study, composite adverse perinatal outcome (CAPO) was defined as the presence of one or more severe neonatal complications. These included an Apgar score below 7 at 5 minutes, the need for NICU admission, respiratory distress, requirement for ventilator support or cardiopulmonary resuscitation, seizures, hypoxic-ischemic encephalopathy (HIE), sepsis, bronchopulmonary dysplasia, necrotizing enterocolitis (NEC), birth injury, perinatal death, or a neonatal arterial blood gas pH below 7.2. The parameters were selected for their clinical relevance in identifying significant neonatal morbidity and mortality.

RESULTS

The demographic details of dichorionic twin pregnancies have been investigated in relation to fetal sex concordance. The maternal age was considerably elevated in the group 1 compared to the group 2 (p=0.005). BMI differed significantly among the groups, with the group 3 having a higher BMI than the group 2 (p=0.039). Gravidity, parity, and the number of living children did not show a significant difference among the groups (p=0.69, p=0.55, and p=0.68, respectively), as presented in **Table 1**. No significant differences were observed among the groups in terms of hemoglobin levels (p=0.60) or the proportion of pregnancies conceived via IVF (p=0.93). The prevalence of diabetic diseases showed a significant difference among the groups (p=0.027). Post-hoc analysis revealed that the incidence of diabetic diseases was significantly higher in group 1 compared to group 2 (p=0.008), and in group 3 compared to group 2 (p=0.008). However, no significant difference was observed between group 1 and group 3. The prevalence of hypertensive diseases did not show any significant difference among the groups (p=0.97).

The outcomes of biometric measurements in dichorionic twin pregnancies based on fetal sex combinations are summarized in **Table 2**. Gestational week did not differ significantly among the groups (p=0.863). The mean birth weights for group 1, group 2, and group 3 were 2182.2±401.7 g, 2033.4±530.6 g, and 2195.3±479.3 g, respectively, with groups 1 and 3 showing higher weights than group 2, though this was not statistically significant (p=0.09). No significant differences were noted for weight discordance (p=0.45). However, biparietal diameter (BPD) in group 3 compared to group 2. Head circumference (HC) and abdominal circumference (AC) was also larger in groups 1 and 3 compared to group 2. Femur length (FL) showed no significant variation (p=0.22). CAPO rates were 44.4% in group 1, 33.3% in group 2, and 40.2% in group 3, without significant differences among the groups (p=0.396).

The comparison of birth weight, gestational age and preterm birth outcomes according to fetal sex concordance in dichorionic twin pregnancies is summarized in **Table 3**. In our study, birth weights of male and female newborns

Table 1. Demographic characteristics according to fetal sex

					Post-hoc comprasions, p-value		
	Group 1 (n=90)	Group 2 (n=56)	Group 3 (n=82)	p	Group 1-group 2	Group 1-group 3	Group 2-group 3
Maternal age (years)	33.0±6.2	30.1±8.6	32.1±5.8	0.005[a]	0.004	NA	NA
BMI (kg/m^2)	30.5±6.6	29.9±5.1	32.5±7.4	0.039[a]	NA	NA	0.049
IVF pregnancy	28.9	26.7	26.8	0.931[b]			
Gravidity	2 (3)	2.5 (3)	2 (3)	0.69[c]			
Parity	1 (2)	1 (1)	1 (2)	0.55[c]			
Living children	1 (2)	1 (1)	1 (2)	0.68[c]			
Hemoglobin g/dl	11.9±1.4	11.2±1.7	11.8±1.3	0.60[a]			
Diabetic diseases	10 (11.1)	0	9 (11.0)	0.027[b]	0.008	NA	0.008
Hypertensive diseases	12 (13.3)	8 (13.3)	10 (12.2)	0.97[b]			

BMI: Body-mass index, IVF: In vitro fertilization, a: One-way ANOVA, b: Chi-square test, c: Kruskal-Wallis test, post-hoc analyses were performed using the Bonferroni correction. Group 1: Male-male, Group 2: Female-female, Group 3: Male-female

Table 2. Birth weight, head circumference, and body length measurements according to fetal sex

					Post-hoc comprasions, p-value		
	Group 1 (n=90)	Group 2 (n=56)	Group 3 (n=82)	p	Group 1-group 2	Group 1-group 3	Group 2-group 3
Gestational age at birth (weeks)	33.88±2.16	33.98±3.13	34.07±2.87	0.863[a]			
Birthweight, g	2182.2±401.7	2033.4±530.6	2195.3±479.3	0.09[a]			
Weight Discordance, g	260 (390)	255 (185)	250 (325)	0.454[b]			
Weight Discordance, %	9.84 (15.88)	8.95 (15.70)	7.86 (10.53)	0.426[c]			
BPD, cm	83 (8)	82 (8)	84 (8)	0.005[b]	NA	NA	0.004
HC, cm	305 (23)	302 (27)	306 (18)	0.009[b]	0.006	NA	0.005
AC, cm	292 (36)	268(53)	300 (39)	0.001[b]	0.001	NA	0.001
FL, cm	64 (9)	62 (9)	65 (8)	0.221[b]			
CAPO	40 (44.4)	20 (33.3)	33 (40.2)	0.396[c]			

BPD: Biparietal diameter, HC: Head circumference, AC: Abdominal circumference, FL: Femur length, CAPO: Composite adverse perinatal outcome. a: One-way ANOVA, b: Kruskal-Wallis test, c: Chi-square test, Group 1: Male-male, Group 2: Female-female, Group 3: Male-female

Table 3. Comparison of birth weight, gestational age, and preterm delivery outcomes between fetal sex groups

	Male from concordant pregnancy	Male from discordant pregnancy	p	Female from concordant pregnancy	Female from discordant pregnancy	p
Birth weight, g	2182.2±401.6	2344.7±478.4	0.04[a]	2033.6±530.3	2052.6±439.9	0.84[a]
LBW	66 (73.3)	27 (67.5)	0.49[b]	54 (90.0)	34 (81.0)	0.19[b]
VLBW	7 (7.8)	3 (7.5)	0.95[b]	11 (18.3)	4 (9.5)	0.22[b]
Gestational age at birth, weeks	33.9±2.1	34.1±2.9	0.72[a]	34.2±3.2	34.1±2.8	0.82[a]
NICU	43 (47.8)	15 (35.5)	0.27[c]	23 (38.8)	19 (45.2)	0.48[c]

LBW: Low birth weight, VLBW: Very low birth weight, NICU: Neonatal intensive care unit, SD: Standard deviation, IQR: Interquartile range, a: Student T test, mean±SD, b: Chi-square test, no (%), c: Mann-Whitney U, median (IQR), Group 1: Male-male, Group 2: Female-female, Group 3: Male-female

born from concordant and discordant pregnancies were compared. Among male newborns, the birth weight of those born from group1 (concordant) pregnancies (2182.2±401.6 g) was significantly lower than that of those born from group 3 (discordant) pregnancies (2344.7±478.4 g) (p=0.04). However, among female newborns, there was no significant difference in birth weight between those born from group 2 (concordant) pregnancies (2033.6±530.3 g) and those born from group 3 (discordant) pregnancies (2052.6±439.9 g) (p=0.84). LBW and VLBW rates did not differ significantly between concordant and discordant pregnancies for both male newborns (p=0.49, p=0.95) and female newborns (p=0.19, p=0.22). The gestational age at birth was also similar between the groups, and no significant difference was found for both male newborns (p=0.72) and female newborns (p=0.82). NICU requirement was also not significantly different between the groups. For male newborns, the need for NICU was similar between concordant and discordant pregnancies (p=0.27). Similarly, there was no significant difference in NICU requirement for female newborns (p=0.48).

DISCUSSION

The impact of fetal sex on maternal health, pregnancy course, and neonatal outcome is a topic of continued investigation. Although several studies have indicated that male and female fetuses can differentially affect the physiological aspects of pregnancy, especially in singleton pregnancies, the magnitude of this effect in twin pregnancies is unclear.[4] Dichorionic twin gestations offer a special model for evaluating these influences since they enable comparison of various fetal sex combinations while controlling for confounding factors such as shared placental circulation.[2] The objective of our research was to evaluate whether concordance or discordance of fetal sex influences maternal metabolic parameters, neonatal growth patterns, and perinatal outcomes. The results contribute to the current scientific body of evidence by demonstrating that fetal sex combinations significantly impact maternal body mass index, metabolic status, and fetal biometric parameters but have a modest effect on perinatal morbidity.

The association of fetal sex with maternal demographic characteristics is a controversial issue in the literature. Previous studies have shown that pregnant women carrying a male fetus are correlated with increased maternal age, increased preterm birth rates and some maternal complications.[5] In our study, maternal age was markedly elevated in the group1 group than group 2 (p=0.005), which supports the findings of the literature. Although there was no significant difference between the groups in terms of BMI values in your own study (p=0.039), it has been reported in the literature that BMI may be associated with fetal sex.[6] For example, it was reported that AKR1C1 expression was higher in pregnant women carrying male fetuses and that this was positively correlated with maternal BMI.[6] Moreover, emerging evidence suggests that fetal sex may influence maternal metabolic adaptation during pregnancy. Retnakaran et al.[7] demonstrated that carrying a male fetus is associated with impaired maternal β-cell function and increased postprandial glycemia, leading to a higher risk of gestational diabetes mellitus (GDM). In their study, women carrying male fetuses exhibited higher blood glucose levels during the oral glucose tolerance test (OGTT) and had a 39% increased risk of developing GDM compared to those carrying female fetuses. These findings align with our results, which indicate that diabetic diseases were significantly more common in group 1 and group 3 twin pregnancies than in group 2 pregnancies (p=0.027). This suggests that fetal sex-related metabolic changes may contribute to maternal glucose dysregulation, further supporting the hypothesis that male fetuses impose a greater metabolic burden on the mother.

Nonetheless, no substantial difference was seen between the groups regarding obstetric history parameters such as IVF pregnancy rates, gravida, parity and number of living children and hemoglobin levels (p: 0.93, p: 0.69, p: 0.55, p: 0.55, p: 0.68 and p: 0.60). Our study revealed no disparities between the groups regarding the prevalence of maternal hypertensive diseases, but diabetic diseases were significantly more common in group 1 and group 3 twin pregnancies than in group 2 pregnancies (p=0.027).

In a study conducted by Muhcu et al.[8] in 2014, which is one of the studies evaluating the effect of fetal sex on ultrasonographic measurements, it was reported that male fetuses had higher values in parameters such as birth weight and HC compared to female fetuses. In addition, HC of male fetuses were found to be larger at 35-40 weeks of gestation. Similarly, another study reported that fetal gender may have an effect on ultrasonographic measurements such as BPD, HC, AC, FL and EFW.[9] In our study, there was no significant difference between the groups in terms of birth weight (p=0.09). However, BPD, HC and AC measurements were larger in group 1 and group 3 compared to group 2 and these differences were statistically significant (p=0.005, p=0.009 and p=0.001). These findings are consistent with the literature suggesting that fetal sex may have an effect on birth weight and ultrasonographic measurements. One possible explanation is that male fetuses exhibit higher insulin-like growth factor-1 (IGF-1) levels and greater anabolic activity, contributing to their increased head and abdominal circumference measurements.[10] Additionally, placental function may differ between male and female fetuses, with studies suggesting that placentas from male fetuses may be more efficient in nutrient transport.[11]

Wilms et al.[12] reported that the majority of preterm births were seen in pregnant women carrying a male fetus and that these pregnant women gave birth earlier.However, secondary analyses showed that there was no significant difference in the risk of preterm birth between women carrying male and female fetuses, with the difference being due to ethnicity. According to this analysis, the median gestational age was 37 5/7 weeks in women carrying a male fetus and 38 1/7 weeks in women carrying a female fetus, but there was no significant difference in risk between the two groups. In the study of Melamed et al.[13] on twin pregnancies, there was no significant difference in terms of gestational age at delivery between different fetal sex combinations. In our study, no significant difference was found between the groups in terms of gestational week (p=0.863). The gestational weeks of gestation in group 1, group 2 and group 3 pregnancies were 33.88±2.16, 33.23±3.13 and 34.07±2.87, respectively. CAPO results showed no significant difference between the groups (p=0.396). Although the CAPO rate appeared to be lower in group 2, no statistically significant difference was found. In the literature, there are some studies in which pregnancies carrying a male fetus are associated with higher neonatal risks.[13] However, the high CAPO rates in all groups in our study may be due to the general obstetric and neonatal characteristics of the studied population; therefore, it is thought that the results should be repeated in a larger population.

In our study, we examined the effect of fetal sex concordance or discordance on pregnancy outcomes. As summarized in **Table 3**, birth weights were compared between male and female newborns born from concordant and discordant pregnancies. Among male newborns, the birth weight of those born from group 1 (concordant) pregnancies was significantly lower than those born from group 3 (discordant) pregnancies (p=0.04). In contrast, among female newborns, there was no significant difference in birth weight between those born to group 2 (concordant) pregnancies and those born to group 3 (discordant) pregnancies (p=0.84). These findings appear to be consistent with some studies in the literature. In the CODATwins study, a large-scale analysis of 67,850 dizygotic twins found that male fetuses were on average 31 g heavier and 0.16 cm longer when they had a female partner than when they had a male partner.[14] However, there was no significant effect of co-twin sex on birth measurements in female fetuses. In addition, the duration of gestation was reported to be shorter in group 1 pairs than in boy-girl and girl-girl pairs. These findings suggest that male fetuses may have a longer gestation period and higher birth size in the presence of a female partner. However, these differences were reported to be attenuated in the presence of birth weight in relation to gestational duration. Similarly, Bayraktar et al.[15] reported that male newborns in male-girl pregnancies had a higher birth weight than male-male pregnancies. In addition, Melamed et al.[13] provided a different perspective, reporting that the growth rate of male fetuses in male-male pregnancies was lower than in male-female pregnancies. In this study, male fetuses showed higher growth rates and longer gestation periods in the presence of a female mate, and hypothesized that male fetuses may have an advantage in competition for food in the presence of a female mate rather than a male mate. However, the mechanisms underlying this observation remain unclear. In contrast, in our study, the birth weight of female newborns born to discordant pregnancies (boy-girl) was slightly higher than that of female newborns born to concordant pregnancies (girl-girl), but this difference was not statistically significant. This finding is consistent with the “girl protective factor” hypothesis proposed in the study by Melamed et al., which states that female fetuses may show better growth dynamics when found with their male twins.

In our study, the NICU needs of newborns in gender concordant and discordant pregnancies were examined and no significant difference was found between the groups (p=0.27 for boys and p=0.48 for girls).

The findings of our study have potential clinical implications for the management of twin pregnancies. Given that male-containing pregnancies (group 1 and group 3) were associated with higher maternal BMI and increased risk of gestational diabetes, closer metabolic surveillance and early screening for gestational diabetes may be warranted in these pregnancies.

Although our study did not find significant differences in perinatal morbidity, future research should explore whether fetal sex concordance impacts long-term neonatal outcomes, including metabolic programming and neurodevelopmental trajectories. The potential influence of fetal sex on placental function and maternal metabolic adaptations also warrants further investigation using molecular and epigenetic approaches.

Limitations

This study has some limitations that should be considered. The relatively small sample size limits the generalizability of our findings, particularly in subgroup analyses based on fetal sex combinations. Second, although we adjusted for confounding variables such as maternal age, parity, and gestational age at delivery, other unmeasured factors, including genetic and environmental influences, may have impacted the outcomes. Finally, the study was conducted in a single center, which may limit the applicability of the results to broader populations. Future prospective, multicenter studies with larger sample sizes are needed to validate our findings and explore the underlying mechanisms of fetal sex-related differences in dichorionic twin pregnancies.

CONCLUSION

This research points to the effects of fetal sex discordance and concordance on neonatal, pregnancy, and maternal outcomes in dichorionic twin pregnancies. The group 1 pregnancies were correlated with increased age of the mother, BMI, parity, and rate of diabetic disease in relation to female-female pregnancies. Neonatal outcome revealed increased biparietal diameter, head circumference, and abdominal circumference in group 1 and group 2 pregnancies, and increased birth weight in male newborns of discordant pregnancies compared to concordant pregnancies. Gestational age, preterm delivery rates, and NICU admission were comparable between groups. These results highlight the effect of fetal sex combinations on neonatal and maternal outcomes. Larger multicenter trials are required to validate these results and to investigate further their implications for maximizing antenatal care in twin pregnancy.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 25.12.2024, Decision No: AEŞH-BADEK-2024-1200).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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