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The relationship of gros anomalies of the umbilical cord with placental pathologies

Göbek kordonu gros anomalilerinin plasenta patolojileri ile ilişkisi

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ABSTRACT

Aim: Within the scope of this research, we aimed to elucidate and compare placental histological features and perinatal outcomes in all deliveries with or without umbilical cord anomaly.

Materials and Methods: Regarding patient groups, 270 cases with cord abnormalities were included in the study group and 835 cases in the control group. Umbilical cord abnormalities: The presence of a true or false knot in the umbilical cord was determined based on the umbilical cord wrapping around the fetal neck and the presence of stenosis. The cases without any umbilical cord abnormalities mentioned in the study group were determined as the control group. All patients' demographic data, prenatal information, intrapartum information, postpartum information, postpartum period, and newborn follow-up were recorded. After delivery, umbilical cord abnormalities and placenta macroscopic and microscopy results were evaluated.

Results: No placental pathology was detected in the control group, but there was a statistical significance between the study and control groups, including fetal vascular thrombosis and ectasia pathology and fetal vasculopathy or avascular villi pathology. There was no difference between the study and control groups regarding preeclampsia, ablatio placenta, and intrauterine fetal demise. Intrauterine growth restriction was detected at a higher rate in the study group, and the difference was significant. No difference was observed between the two groups regarding Apgar scores *1st* and *5th*min of newborns and the requirement for hospitalization in the neonatal intensive care unit. **Conclusion:** Gros cord anomalies, fetal vascular ectasia and thrombosis, and fetal thrombotic vasculopathy lead to pathologies associated with placental insufficiency, suggesting that it is an independent risk factor for intrauterine growth restriction.

Keywords: Cord anomaly, intrauterine maternal loss, intrauterine growth restriction, apgar score, newborn.

ÖZ

Amaç: *Bu araştırma kapsamında göbek kordonu anomalisi olan ve olmayan tüm doğumlarda plasentanın histolojik özelliklerin ve perinatal sonuçların aydınlatılması ve karşılaştırılması amaçlandı.*

Gereçler ve Yöntem: *Hasta gruplarına bakıldığında çalışma grubunda 270, kontrol grubunda 835 olgu yer aldı. Kordon anormalliği olanlar çalışma grubuna dahil edildi. Göbek kordonu anormallikleri; Kordonda gerçek ya da yalancı düğüm olması, göbek kordonunun fetal boyun çevresine dolanması ve kordonda darlık varlığı olarak belirlendi. Çalışma grubunda adı geçen herhangi bir göbek kordonu anormalliği olmayan olgular kontrol grubu olarak belirlendi. Tüm hastaların demografik verileri, prenatal bilgileri, intrapartum bilgileri, postpartum bilgileri, postpartum dönemleri ve yenidoğan izlemleri kaydedildi. Doğumdan sonra göbek kordonu anormallikleri ve plasenta makroskobik ve mikroskopi sonuçları prospektif olarak izlendi.*

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Bulgular: *Kontrol grubunda plasenta patolojisi saptanmadı, ancak çalışma grubunda fetal vasküler tromboz ve ektazi patolojisi ve fetal vaskülopati veya avasküler villus patolojisi gibi anormalikler daha fazla izlendi. Çalışma ve kontrol grupları arasında preeklampsi, plasenta dekolmanı ve intrauterin fetal kayıp açısından fark yoktu. Çalışma grubunda intrauterin gelişme geriliği daha yüksek saptandı ve aradaki fark anlamlıydı. Yenidoğanların 1. ve 5. dakika Apgar skorları ve yenidoğan yoğun bakım ünitesinde yatış gerekliliği açısından iki grup arasında fark izlenmedi.*

Sonuç: *Gros kordon anomalileri, fetal vasküler ektazi ve tromboz ve fetal trombotik vaskülopati plasenta yetmezliği ile ilişkili patolojilere yol açarak intrauterin gelişme geriliği için bağımsız bir risk faktörü olduğunu düşündürmektedir.*

Anahtar Sözcükler: *Kordon anomalisi, intrauterin fetal kayıp, intrauterin gelişme geriliği, apgar skoru, yenidoğan.*

INTRODUCTION

The umbilical cord is an important structure that plays a critical role in the life of the developing fetus, both structurally and functionally, that provides the relationship between the fetus and the placenta. Generally, ultrasonographic examinations of the umbilical cord were based on the number of vessels and Doppler blood flow. There is limited information about the effects of prenatal umbilical cord morphology on the fetus in the prenatal period and the newborn in the postnatal period. The results of a limited number of studies have shown that umbilical cord morphology and its components affect the pregnancy process, mode of delivery, and outcome (1, 2).

Although the umbilical cord is the only organ that disappears afterlife begins, it is the most important component of the fetoplacental unit. It plays a decisive role in the onset of extrauterine life. Fetal growth and development are characterized by differentiation, maturation, and growth of fetal tissues and organs (3). The main factors affecting fetal growth and development are genetic structure, uteroplacental function, and maternal environment. Under conditions where all these factors are favorable, a healthy fetus completes its intrauterine somatic growth. If the conditions are not suitable, fetal growth and development may be adversely affected and limited. Abnormal maternal, fetal, and placental factors may adversely affect fetal growth and development individually or together (4, 5).

Clinical experience and experimental evidence have shown that the morphology and components of the umbilical cord affect the pregnancy process, mode of delivery, and outcome (6). Many researchers reported that altered umbilical cord morphology is associated with hypertensive disorders, fetal distress, gestational diabetes, fetal growth restriction, and intrapartum complications. They altered umbilical vein blood flow in the second and third trimesters (2). The genetic and physiological factors predisposing to complications related to the umbilical cord are not yet clearly understood. However, the localization of some maternal factors, abnormal cord insertion and morphology, and cord length can be considered among the possible causes. Vital dysfunction of the umbilical circulation is suspected in at least 20% of autopsy examinations of stillbirths (7). Any force that compresses the cord may reduce blood flow to the umbilical vessels and cause fetal hypoxia and circulatory dysfunction. Mechanical cord compression or 'cord accident' can be caused by cord entanglement or prolapse, as well as abnormal cord structures such as true knots, hyper coiling, abnormally long cord, abnormal cord insertion, and cord stenosis (8).

Parast et al. (9) demonstrated that non-acute umbilical cord occlusion is associated with congestion and stasis resulting from umbilical vein compression and also included thrombosis, ectasia of large vessels in the placenta, and avascularity in terminal chorionic villi. The condition formerly called fetal thrombotic vasculopathy (FTV) has been associated with poor perinatal outcomes, including stillbirth and neurological damage (10). Tantbirojn et al. (11) reported that thrombosis and fetal thrombotic vasculopathy were specific for stillbirths originating from the umbilical cord.

Within the scope of this research, we aimed to elucidate and compare placental histological features and perinatal outcomes in all deliveries with or without umbilical cord anomaly.

MATERIALS and METHODS

A total of 1105 females who had a delivery in our institution have been enrolled in this prospective study. Regarding patient groups, 270 cases with cord abnormalities were included in the study

group and 835 cases in the control group. Umbilical cord abnormalities: The presence of a true or false knot in the umbilical cord was determined based on the umbilical cord wrapping around the fetal neck and the presence of stenosis. The cases without any umbilical cord abnormalities mentioned in the study group were determined as the control group. All patients' demographic data, prenatal information, intrapartum information, postpartum information, postpartum period, and newborn follow-up were recorded. After delivery, umbilical cord abnormalities and placenta macroscopic and microscopy results were evaluated. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution, and informed consent has been obtained from all participants.

Age, height, weight, arterial blood pressure, gestational week values, and previous pregnancy status of 1105 cases participating in the study were evaluated regarding complications with preeclampsia, ablation placenta, placenta previa, intrauterine growth restriction (IUGR), intrauterine fetal loss (IUFL). As intrapartum period records the week of delivery, the amount of amniotic fluid in the last stage of pregnancy, the birth weight of the baby, the weight of the placenta, the status of the amniotic fluid or placenta stained with meconium during delivery, the last non-stress test (NST) reactivity before delivery and the mode of delivery data were recorded. but there was a statistical significance between the study and control groups

During birth, anomalies detected such as length or shortness of the umbilical cord, presence of stenosis, presence of real or false knot, coil index, and wrapping of the umbilical cord around the fetal neck were recorded.

As postpartum fetal information, 1st and 5th-minute APGAR scores have been obtained. Babies with low Apgar results were transported to the neonatal intensive care unit (NICU).

The pathological examination of the two samples taken from the placental parenchyma has been transferred to the pathology department for investigation. The samples were taken from a region close to the umbilical cord insertion and placental membranes.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) 13 program was used for the data analysis. The mean value was calculated for those with normal distribution among the numerical variables, and a t-test was performed for statistical analysis. The chi-square test was utilized to compare the meaning of qualitative data between groups. The results were evaluated at the 95% confidence interval and the significance level of $p<0.05$.

RESULTS

A total of 1105 pregnant women (835 in the control group and 270 in the study group) were included in this prospective research. In the study group, fetal neck cord entanglement was observed in 120 cases, coil index anomaly in 112 cases, false knot anomaly in 60 cases, long umbilical cord abnormality in 18 cases, true knot anomaly in 15 cases, and no umbilical cord stricture abnormality was observed in any individual.

The median birth week of the cases in the study group was 37.4, and the control group was 37.9 weeks. Birth median weight in the study group was 2938 gr. And 3035 g in the control group. The median placenta weight was 564 g in the study group. 564 gr in the control group. A statistically significant difference was observed between the study and control groups regarding the birth week (p:0.017). In contrast, no statistically significant difference was found in terms of newborn birth weight and placental weight.

During the pathological examination, the normal placenta was detected in 804 (72.8%) cases, chorangiosis in 168 (15.2%) cases, fetal vascular thrombosis and ectasia in 126 (11.4%) cases, fetal vasculopathy, and avascular villi in 7 (0.6%) cases. There were 193 (71.5%) cases in the study group with normal pathology results and 611 (73.2%) cases in the control group. The normal placenta detection rate was higher in the control group than in the study group, and the difference was statistically significant. There were 33 cases in the study group regarding fetal vascular thrombosis and ectasia pathology and 93 cases in the control group, and the difference was statistically significant (Figure-1 & Figure-2).

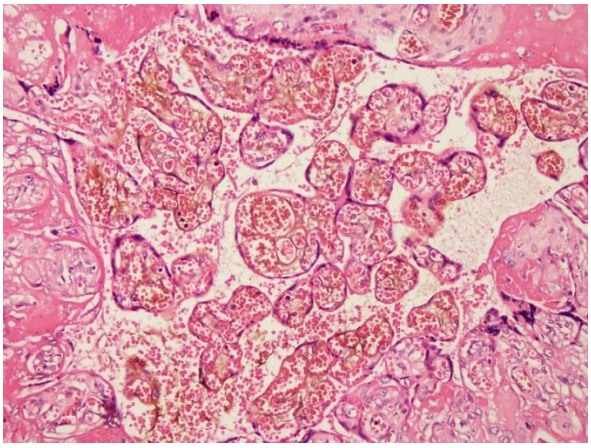

Figure-1. *Chorangiosis.*
Terminal chorionic villi containing ten or more capillary vessels are seen in at least ten terminal villi in the hematoxylin-eosin-stained preparation (x40 magnification).

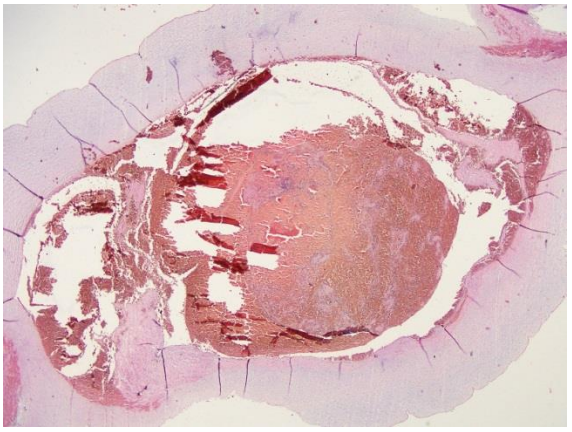

Figure-2. *Vascular thrombosis and ectasia.*
In the hematoxylin-eosin-stained preparation (in x10 magnification), a vessel with dilatation at least four times the diameter of the surrounding umbilical artery and/or vein, and the endothelial integrity of the tunica intima layer is partially disrupted by the organized thrombus.

It was determined that 70 (6.3%) of the 1105 cases included in the study were complicated by IUGR. Of these, 39 cases were diagnosed as early IUGR, and 31 were diagnosed as late IUGR. It was revealed that there was a statistically significant difference between the study and control groups in terms of complicating pregnancy with IUGR(p<0.02). It was observed that the cases in the study group were more complicated with IUGR (Table-1).

When the Apgar scores and the requirement for NICU were interpreted at the 1st and 5th minutes, the 1st minute Apgar score was ≥7 in 874 (79.1%) of the cases, within normal limits. The Apgar score was between 4 – 7 in 203 (18.4%) cases and 4≥ in 28 (2.5%) cases. There was no statistical difference between the study and control groups regarding the Apgar score (p=0.320). The 5th minute Apgar score was ≥7 in 1062 (96.1%) cases, between 4 – 7in 38 cases, and 4≥ in 5 cases, with no difference between the groups (p=0.353) (Table-2).

Table-1. Comparison of clinical conditions complicating pregnancy.

	Study Group	Control Group	P-value
Preeclampsia	15 (5.5&)	38 (4.5+)	0.756
IUGR	25 (9.3%)	45 (5.4%)	0.020*
IUML	1 (0.4%)	2 (0.2%)	0.567
Ablatio plasenta	3 (1.1%)	9 (1.1%)	1.000

(*p<0.05)

Table-2. Comparison of newborn findings.

	Study Group	Control Group	P-value
1. Minute Apgar score	56(20.7%)	175(21.0%)	0.320
5. Minute Apgar score	14(5.2%)	29 (3.5%)	0.353
Newborn Hospitalization	40 (14.8%)	107 (12.8%)	0.701
Exitus	1 (0.4%)	3 (0.4%)	1.000

(*p<0.05)

We evaluated the intrapartum variables regarding amniotic fluid at the time of delivery, whether the amniotic fluid was stained with meconium at birth, NST reactivity at the time of delivery, and mode of delivery. The amniotic fluid was within normal limits according to the gestational week in 983 (89.0%) cases, oligohydramnios was found in 105 (9.5%) cases, and polyhydramnios was in 17 (1.5%) cases. There was no statistically significant difference between the study and control groups in terms of normal amniotic fluid at the time of delivery, polyhydramnios, or oligohydramnios (p=0.200).

The rate of cesarean sections was higher in the study group than controls, but the difference was insignificant.

DISCUSSION

In parallel with the increasing use of ultrasonography in perinatal processes, clinical practice and research focus more on the fetus.

Ultrasonographic applications related to the umbilical cord are mostly limited to determining the number of vessels and evaluation of umbilical artery and vein Doppler blood flow (12). However, the important role of the placenta and umbilical cord in regulating fetal development cannot be denied. Studies on the umbilical cord have shown that it and its components are effective in pregnancy and neonatal outcomes. Current studies draw attention to intrauterine loss, gestational diabetes, preeclampsia, intrauterine growth restriction, fetal distress during delivery, and the relationship between fetuses with meconium and umbilical cord (13).

Benirschke emphasized the association with umbilical cord pathologies such as long and short umbilical cord, velamentous insertion, umbilical cord knot, and poor newborn outcomes (14). Collins stated that there may be a relationship between umbilical cord abnormalities and unexpected neonatal deaths (15). Naeye mentioned the association of short umbilical cord abnormality with low Apgar score, low IQ, and neurological abnormalities (16). Peng et al. stated that umbilical cord stricture and hyper coiling abnormalities cause fetal death (17). In our study, a statistically significant difference was detected in the pathological findings in terms of fetal vascular thrombosis and ectasia pathology in the control group and the study group. For this reason, In our study investigating non-acute obstruction of the umbilical cord as a predisposing cause for poor pregnancy outcomes, findings related to vascular congestion and stasis were associated with neonatal morbidity and mortality.

Previous literature reported that decreased fetal movements and changes in fetal cardiac rate may be signs of intrauterine asphyxia in the advanced stages of pregnancy. Umbilical cord-related complications accompany fetal asphyxia with a rate of 5 – 18% and still births of 10 – 12% (18). Morrison et al. reported cord complications in 48% of asphyxia newborns at term (19).

The cord pathologies and neonatal pathologies have been comprehensively elaborated. Machin et al. emphasized the connection between abnormal umbilical coil index and intrauterine fetal death and intrauterine growth restriction (20), Naeye et al. stated that umbilical cord length could be affected by many factors such as maternal weight, pre-pregnancy weight, socioeconomic status, and infant weight, and that umbilical cord abnormality is associated with psychomotor restriction. It has been reported that it may be related (16). In another study, a relationship was found between the long umbilical cord and infant development, and an increased risk of fetuses with abnormal neurologic development was reported in subsequent pregnancies (21). Airas et al. conducted a study of 23.315 cases and found a significant relationship between true knots in the umbilical cord and stillbirth and low 1st-minuteApgar score (22). Rhoades et al. stated that cord entanglement is an independent risk factor for delivery. Their study revealed that although cord entanglement to the fetal neck poses a risk for perinatal problems, it does not affect the length of hospital stay (23).

Tantbirojn et al. (11) focused on fetal blood flow-limiting vascular changes other than cord entanglement. They evaluated histological features in their study, in which fetal vascular ectasia, fetal vascular thrombosis, fetal thrombotic vasculopathy (avascular villi, villous stromal choriorexis, and their combinations) were found in cases of a bad pregnancy, especially IUGR. The fetal thrombotic vasculopathy was associated with gross umbilical cord anomaly in stillbirth cases. A close relationship has been reported between fetal thrombotic vasculopathy and stillbirth (24). A massive fetal thrombotic vasculopathy is detected in approximately 50% of stillbirth placentas. On the other hand, Larson et al. (25) examined 13.895 pregnant women and found the rate of cord entanglement in the 20th week to be 5.8% and 29% in the 42nd week.

Chorangiosis is defined by numerous enlarged, highly vascular villi throughout the placenta. However, chorangiosis is a nonspecific change associated with maternal diabetes, hypertension, infections, anomalies, intrauterine fetal death, and growth restriction.

In our present study, while a significant relationship was found between cord pathologies and IUGR, no significant difference was found for preeclampsia, intrauterine fetal loss, and ablatio placenta. Cord pathologies were found to be an independent risk factor for IUGG rather than other poor pregnancy outcomes. When the placental pathology results were examined, we found the frequency of chorangiosis to be similar. However, placental pathology results evaluated as fetal vascular ectasia and thrombosis, fetal thrombotic vasculopathy, and avascular villi were

found to be statistically significant in the study group.

In our study, the relationship between umbilical cord entanglement in the fetal neck, umbilical cord coil index abnormality, and false node abnormalities with placental pathologies was more evident in the cases in the study group.

When the study and control groups were evaluated regarding newborn outcomes, no significant difference was found in terms of 1st and 5th-minuteApgar scores and the requirement for hospitalization in the neonatal intensive care unit. In addition to perinatal outcomes such as intrauterine death, prematurity, the tendency to neonatal complications, neuromotor developmental defects, and IUGR also paves the way for diseases such as diabetes, cardiovascular diseases, and depressive disorders that are reflected in adult life (26).

These results are associated with impaired fetal programming and delayed fetal life maturation due to IUGR. Therefore, although the 1st and 5th-minute Apgar scores of the newborn in cases with gross umbilical cord anomalies are similar to the cases in the control group, the significantly higher neonatal morbidity and mortality in the study group can be explained by chronic placental insufficiency.

Gross cord anomalies such as fetal neck cord entanglement, long or short cord, hyper coiling or hypo coiling false or true knot, and cord stricture are associated with stillbirth IUGR, intrapartum and postpartum complications. Stasis-related changes in fetal vessels and chorionic villi in placental microscopic evaluations were significantly increased in cases with gross cord anomaly, and the increase in poor perinatal outcomes, especially in IUGR, is remarkable. Gross cord anomalies are an independent risk factor for IUGR by causing pathologies associated with placental insufficiency, such as fetal vascular ectasia and thrombosis, and fetal thrombotic vasculopathy. In addition, no significant difference was observed between the 1st and 5th minute Apgar scores of the postpartum newborn, while high morbidity and mortality were detected in the follow-up of the newborn.

CONCLUSION

In order to evaluate the presence of thrombosis and fetal thrombotic vasculopathy, especially in gross anomalies predisposing to vascular occlusion, it seems necessary to send all placentas for pathological examination, including adequate sampling from large fetal vessels and placental parenchyma. For this, giving the placenta and cord the value they deserve after birth is necessary to carry out their macroscopic examination meticulously. Even if the placenta is macroscopically normal after birth, it should be routinely subjected to histopathological examination, especially when conditions that are thought to be associated with poor obstetric outcomes are detected during antenatal follow-up. In this way, placental histopathology can contribute to the planning and management of subsequent pregnancies by revealing the causes of poor pregnancy outcomes.

Conflict of interest: All authors participating in the study declare that there is no conflict of interest regarding the study.

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