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# **ORIGINAL ARTICLE**

# Outcomes and Management of Pregnancies Complicated by Absent End-Diastolic Flow in the Umbilical Artery: A Retrospective Cohort Study

# Umbilikal Arterde Diyastolik Akım Kaybı ile Komplike Gebeliklerin Sonuçları ve Yönetimi: Retrospektif Kohort Çalışması

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#### ABSTRACT

Aim: This study aimed to evaluate perinatal outcomes in pregnancies complicated by absent end-diastolic flow (AEDF) in the umbilical artery. Method: This retrospective cohort study was conducted in the Perinatology Clinic of Etlik City Hospital from November 2022 to June 2024. Eighty-five pregnant women diagnosed with AEDF in the umbilical artery Doppler were included. Key outcomes, including fetal birth weight, gestational age at delivery. Apgar scores, neonatal intensive care unit (NICU) admissions, and perinatal morbidity and mortality, were assessed. **Results:** The mean gestational age at diagnosis and delivery was 28.86 ± 4.00 and 29.74±3.85 weeks, respectively, with a median interval from AEDF detection to delivery of two days. The mean birth weight was 1031.42±485.94 grams. A high cesarean delivery rate (89.4%) was observed, primarily due to fetal distress (63.2%). Fetal growth restriction (FGR) and preeclampsia were present in 80% and 38.8% of cases, respectively. The perinatal loss was 32.9%, with significant associations between higher hCG MoM levels and lower birth weight (r=-0.597, p=0.011). ROC analysis indicated gestational age at delivery as the strongest predictor of neonatal complications, including intracranial hemorrhage (ICH) and respiratory distress syndrome (RDS), aligning with the risk of poor outcomes in AEDF cases. **Conclusion:** AEDF in the umbilical artery is a significant predictor of adverse perinatal outcomes,

**Conclusion:** AEDF in the umbilical artery is a significant predictor of adverse perinatal outcomes, including high perinatal mortality and neonatal complications. Early detection and careful monitoring, alongside timely delivery, are critical in managing these high-risk pregnancies to improve neonatal outcomes. Further research should focus on optimizing intervention timing to balance fetal maturity with the risks of prematurity.

Keywords: Absent end-diastolic flow, fetal ultrasound, perinatal outcomes

### ÖZ

Amaç: Bu çalışma, umbilikal arterde son diyastolik akım (AEDF) kaybıyla komplike olmuş gebeliklerde

Amaç: Di çalişinla, Umbilikal arte de son alyasıdık kalim (AEDF) kaybıyla kompilke olinlış gebeliklerde perinatal sonuçları değerlendirmeyi amaçlamıştır.
Yöntem: Bu retrospektif kohort çalışma, Kasım 2022 ile Haziran 2024 tarihleri arasında Etlik Şehir Hastanesi Perinatoloji Kliniği'nde yürütülmüştür. Umbiliklal arter Doppler incelemesinde AEDF tanısı konulan 85 gebe çalışmaya dahil edilmiştir. Değerlendirinen temel sonuçlar arasında fetal doğum ağırlığı, doğum haftası, Apgar skorları, yenidoğan yoğun bakım (YYB) başvuruları ve perinatal morbidite ile mortalite yer almaktadır.

norbilite ile mortalite yer almaktadir. **Bulgular:** Tani ve doğum sırasında ortalama gebelik haftası sırasıyla 28.86±4.00 ve 29.74±3.85 hafta olup, AEDF tespitinden doğuma kadar geçen sürenin medyan değeri iki gündü. Ortalama doğum ağırlığı 1031.42±485.94 gram olarak bulunmuştur. Yüksek sezaryen oranı (%89.4) gözlenmiş olup, ana neden fetal distres (%63.2) olarak belirlenmiştir. Olgulann %80'inde fetal büyüme geriliği (FGR) ve %38.8'inde preeklampsi mevcut olup, perinatal kayıp oranı %32.9 olarak saptanmıştır. Yüksek hCG MoM seviyeleri ile düşük doğum ağırlığı arasında anlamlı bir ilişki bulunmuştur (r=-0.597, p=0.01). ROC analizinde, doğum haftasının neonatal komplikasyonlar için en güçlü öngörücü olduğu görülmüştür (Area under curve (AUC): 0.804]. YYB'ye alınan yenidoğanlarda, intrakraniyal kanama ve solunum sıkıntsı sendromu gibi ciddi neonatal komplikasyonlar gözlenmiş olup, AEDF olgularında kötü sonuç riskinin yüksek olduğu görülmüştür. **Sonuç:** Umbilikal arterde AEDF varlığı, yüksek perinatal mortalite ve neonatal komplikasyonları içeren olumsuz perinatal sonuçların önemli bir belirlevicisidir. Erken tanı ve dikkatli izlem, yanı sıra zamanında doğum, bu yüksek riskli gebeliklerin yönetiminde neonatal sonuçları iyileştirmek için kırtik önemdedir. İleri araştırmalar, prematürite riskleri ile fetal olgunluk arasındaki dengeyi optimize etmek için müdahale zamanlamasının iyileştirilmesine odaklanmalıdır.

etmek için müdahale zamanlamasının iyileştirilmesine odaklanmalıdır

Anahtar Kelimeler: Fetal ultrason, perinatal sonuclar, son divastolik akım kaybı

### Introduction

is associated with significant perinatal morbidity and studies (3). mortality (2). Using Doppler ultrasonography of the

The absence of end-diastolic flow (AEDF) as seen in umbilical artery provides very important information the umbilical artery Doppler pattern or waveform data about the fetal-placental circulation. Being a key factor display is a crucial indication of fetal growth restriction in monitoring fetal well-being during gestation, aberrant (FGR) and placental insufficiency (1). A common results like the lack of AEDF or reversal of end-diastolic finding in pregnancies was considered high-risk flow (AREDF) have been associated with pregnancy situations where complications are more likely to arise. outcomes including premature delivery and low birth FGR, especially when detected early in pregnancy, weight. This can also lead to fetal demise according to



Research has indicated that adverse outcomes like stillbirth and infant death occur frequently when there is a loss of end-diastolic flow detected before the 30th week of pregnancy (4). Deciding when to deliver a baby in the presence of this flow issue is a task as it involves balancing the well-being of the fetus with the risks associated with premature birth. In situations where FGR begins early in pregnancy the likelihood of fetal health problems and loss, during pregnancy rises if Doppler abnormalities are also present (3). The Trial of Randomized Umbilical and Fetal Flow in Europe (TRUFFLE) study examined cases with Doppler abnormalities in early (26-32 weeks) FGR cases. These abnormalities are linked to higher rates of perinatal health issues and mortality and pose an increased risk, for unfavorable outcomes. As highlighted by the study results close monitoring and making timely decisions regarding delivery play a crucial role in enhancing the well-being of both the fetus and newborn (5).

Our research focuses on assessing the pregnancy results of a group of individuals with no end diastolic flow in the artery who are receiving care at our clinic. Through analyzing these outcomes we aim to add to the increasing amount of research on the effective approaches for managing pregnancies, at high risk.

# **Materials And Methods**

Study Design and Population: This was a retrospective cohort study conducted at Etlik Şehir Hastanesi Perinatoloji Kliniği between November 2022 and June 2024. Approval was received for this study from the Etlik Zübeyde Hanım Gynecology Training and Research Hospital Scientific Research Ethics Committee (Decision No: AE§H-BADEK-2024-950, Date: 16/10/2024). The study included pregnant women diagnosed with absent end-diastolic flow (AEDF) in the umbilical artery during fetal Doppler ultrasound (US) screening. The inclusion criteria were singleton pregnancies, confirmed absent EDF on at least one Doppler US, and availability of comprehensive followup data through delivery. Patients with multiple gestations, major congenital anomalies, or incomplete medical records were excluded from the study.

A total of 85 pregnant women met the inclusion criteria and were followed for pregnancy outcomes, including fetal birth weight, gestational age at delivery, Apgar scores, neonatal intensive care unit (NICU) admission, perinatal morbidity, and mortality.

Data Collection: Data were extracted from the medical records of the patients, including demographic information (maternal age, parity, pre-existing medical conditions), obstetric history, and Doppler US findings. In this study, certain data points were unavailable due to logistical or clinical circumstances. For example, in some cases, specific tests or measurements were not ordered, or delivery occurred before the necessary

data could be collected. To maintain the integrity of the statistical analysis, cases with missing data for key variables were excluded from the relevant analyses. This approach ensured that the results accurately reflect the available data and reduce the potential biases introduced by incomplete datasets.

**Doppler US Protocol:** Absent EDF was identified via Doppler ultrasonography, performed using the Voluson S10 Expert machine with a 3.5 MHz transducer. All Doppler US examinations were performed by experienced sonographers. The umbilical artery Doppler waveform was assessed at the free loop of the cord, and the angle of insonation was kept below 60 degrees. Doppler indices including the pulsatility index (PI), resistance index (RI), and the systolic-to-diastolic ratio (S/D ratio) were recorded. EDF was classified as normal, decreased, absent, or reversed based on the presence or absence of forward diastolic flow.

Statistical Analysis: Data were analyzed using [The Statistical Package for Social Sciences Software, e.g., SPSS, R]. Continuous variables were expressed as mean±standard deviation (SD), and categorical variables were reported as frequencies and percentages. The chi-square or Fisher's exact tests were used for categorical variables, and the student's t-test or Mann-Whitney U test was applied for continuous variables, as appropriate. A p-value of <0.05 was considered statistically significant.

# Results

In this study involving 85 patients, 79 had singleton pregnancies and six had twin pregnancies. The average maternal age was 31.25 years with a standard deviation of 5.74 years. The mean body mass index (BMI) was 30.07, indicating an overweight status. The median gravidity was 2.0, with a range from one to nine pregnancies, while the median parity was 1.0, ranging from 0 to four live births. On average, patients had 1.0 living children, with a range from 0 to four. Six patients, representing 7.06%, conceived through in vitro fertilization (IVF). Among the 18 patients with available 24-hour urine protein levels, the median protein level was 1885 mg, with a range from 176 to 11519 mg. Antihypertensive medications were reported by 29 patients, accounting for 39.7% of the total. Additionally, 76 patients (89.4%) had cesarean deliveries (Table 1).

**Table 1.** Maternal Characteristics of Patients with UmbilicalAbsent End-Diastolic Flow

Variables	n	Values
Maternal Age (years)	85	31.25±5.74
BMI (kg/m²)	85	30.07±5.94
Gravidity	85	2.0 (2) (1-9)
Parity	85	1.0 (2) (0-4)

Living Children	85	1.0 (2) (0-4)
Abortions (min-max)	85	0.0 (0) (0-5)
IVF Pregnancies (%)	85	6 (7.06%)
24-Hour Urine Protein Level (mg)	18	1885 (176- 11519)
Antihypertensive Medication Use (%)	85	29 (39.7)
Cesarean Delivery (%)	85	76 (89.4%)

BMI: Body mass index, kg: Kilograms,  $m^2$ : Square meter, IVF: In vitro fertilization; mg: Milligram

Table 2 presents the maternal and neonatal characteristics of patients with umbilical AEDF. The gestational age at diagnosis was 28.86±4.00 weeks, while the gestational age at delivery was 29.74±3.85 weeks. The interval from the first detection of umbilical AREDV to delivery averaged two days, with a range of 0 to 62 days. The mean birth weight was 1031.42±485.94 grams. The perinatal loss occurred in 31 cases (38.9%), and abnormal ductus venosus waveform was noted in 6 patients.

 Table 2. Maternal and Neonatal Characteristics of Patients

 with Umbilical Absent

### End-Diastolic Flow

Gestational age at diagnosis (weeks)	28. 86±4.00
Gestational age at delivery (weeks)	29.74±3.85
The interval from 1st detection of um- bilical AEDF to delivery (days)	2 (0-62)
Fetal gender	
Female	34 (40)
Male	51 (60)
Birth weight (grams)	1031.42±485.94
Betamethasone administration	76 (90.5)
MgSO4 administration	68 (80)
Apgar score at minute 1	5 (0-9)
Apgar score at minute 5	7 (0-10)
Perinatal Loss	28 (32.9)
Terminaiton of Pregnancy	5 (5.9)
Abnormal Ductus Venosus Waveform	6

AEDF: Absent End-Diastolic Flow, MgSO4: Magnesium Sulfate

FGR was the most prevalent condition, observed in 68 cases (80%). Additionally, Preeclampsia was noted in 33 cases (38.8%). Oligohydramnios was identified in 18 patients (21.2%), while Anhydramnios occurred in seven cases (8.2%) (Table 3).

Table 3. Accompanying Pathological Findings in Patients

Accompanying Pathological Findings	n (%)
FGR	68 (80)
GHT	9 (10.6)
Preeclampsia	33 (38.8)
Chronic Hypertension	5 (5.9)

DM or GDM	6 (7)
Oligohydramnios	18 (21.2)
Polyhydramnios	2 (2.4)
Anhydramnios	7 (8.2)

FGR: Fetal growth restriction, GHT: Gestational hypertension, DM: Diabetes mellitus, GDM: Gestational diabetes mellitus

The most common reason was fetal distress, accounting for 48 cases (63.2%). Other indications included severe preeclampsia (12 cases, 15.8%), HELLP syndrome (six cases, 7.9%), and 34 weeks of gestation, where we decided to deliver electively in cases of umbilical AEDF (Table 4).

Table 4. Cesarean Indications

Cesarean Indication	n (%)
Fetal distress	48 (63.2)
Severe preeclampsia	12 (15.8)
HELLP syndrome	6 (7.9)
Previous uterine scar in labor	1 (1.3)
34 weeks of gestation	8 (10.5)
Placental abruption	1 (1.3)

HELLP: Hemolysis, elevated liver enzymes, and low platelet count

Eighteen patients underwent first-trimester screening, seven patients underwent amniocentesis, among which one case of trisomy 21 was identified. In the correlation analysis, a statistically significant negative relationship was found between birth weight and hCG MoM (r=-0.597, p=0.011). This result indicates that as hCG MoM levels increase, birth weight decreases. No significant relationship was detected between PAPP-A MoM and birth weight (r=-0.098, p=0.708). Additionally, although a moderate positive correlation was observed between hCG MoM and PAPP-A MoM (r=0.449), this relationship did not reach statistical significance (p=0.070).

Among the 85 cases, four patients were diagnosed with AEDF and early-onset FGR at 22-23 weeks of gestation, for which poor prognosis information was provided. Following the request of the family, the termination of pregnancy was performed. Additionally, two cases subsequently resulted in intrauterine demise. The perinatal loss occurred in 28 (32.9). A total of 79 cases were admitted to NICU. During the follow-up at NICU, one or more complications were observed in 14 cases. Specifically, four cases of intracranial hemorrhage (ICH), two cases of sepsis, one case of bowel perforation, one case of portal vein thrombosis, one case of meningitis, and four cases of respiratory distress syndrome (RDS) were noted. Among the surviving neonates, cerebral palsy developed in one case, and retinopathy of prematurity (ROP) was diagnosed in three cases during follow-up. Additionally, one case was diagnosed with Down syndrome postnatally, and

one case was found to have aortic coarctation on postnatal echocardiography.

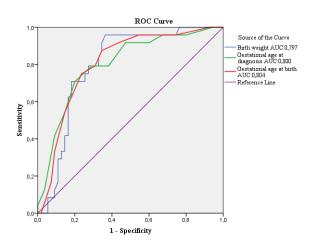
**Table 5.** Correlation Matrix of Birth Weight, hCG MoM, andPAPP-A MoM

Variables	Birth Weight	hCG MoM	PAPP-A MoM
Birth Weight	1	-0.597*	-0.098
hCG MoM	-0.597*	1	0.449
PAPP-A MOM	-0.098	0.449	1

\*Correlation is significant at the 0.05 level (2-tailed). hCG MoM: Human chorionic gonadotropin multiple of the median; PAPP-A MoM: Pregnancy-associated plasma protein-A multiple of the median

In this study, birth weight, gestational age at diagnosis, and gestational age at birth were evaluated with the ROC curve to predict neonatal complications (Figure). The results showed that gestational age at birth (AUC: 0.804) was the strongest predictor. Gestational age at diagnosis (AUC: 0.800) was also an effective predictor but performed slightly less well than gestational age at birth. Birth weight (AUC: 0.797) had a lower predictive power than others; however, the weight was still found to be significant. All parameters showed significant predictive power compared to random guesses.

**Figure.** ROC Curve Analysis for Predicting Neonatal Complications Based on Birth Weight, Gestational Age at Diagnosis, and Gestational Age at Birth



### Discussion

The study found that most patients experienced FGR (80%) and a significant number were diagnosed with preeclampsia (38/8%). The high rate of cesarean deliveries (89/4%) indicated the seriousness of the clinical situations with fetal distress being the main reason in 63/3. Among patients with first-trimester screening data, a significant negative correlation between hCG MoM levels and birth weight was detected.

In this study, we examined perinatal outcomes in pregnancies complicated by the loss of end-diastolic

flow in the umbilical artery. AEDF was diagnosed at an average of 28.86 weeks and birth occurred at 29.74 weeks. The median time to birth with AEDF detection was two days. Our rate of antenatal steroid application for fetal neuroprotection was 90.5% and magnesium sulfate was 80%. The average birth weight was quite low at 1031.42 grams and the perinatal mortality rate was found to be high (32.9%). The study found that most patients experienced FGR (80%) and a significant number were diagnosed with preeclampsia (38/8%). The high rate of cesarean deliveries (89/4%) indicated the seriousness of the clinical situations with fetal distress being the main reason in 63/3. Among patients with first-trimester screening data, a significant negative correlation between hCG MoM levels and birth weight was detected.

Detection of end-diastolic flow in the umbilical artery using Doppler velocimetry serves as a crucial indicator of placental insufficiency in fetuses experiencing growth restriction. AEDF indicates higher vascular resistance in the placental region, which affects fetal blood flow during the diastolic phase of the heart (6). This condition is closely linked to adverse perinatal outcomes, such as higher rates of intrauterine mortality, neonatal health problems, and neonatal mortality. The presence of end-diastolic flow often precedes observable signs of fetal distress providing an opportunity, for early intervention to mitigate potential complications (7).

When maternal demographic data were examined, the mean maternal age was 31.25 (SD 5.74), the mean BMI was 30.07, and the mean gestational age was 28.86±4.00 weeks. In a similar study by Kinoshita et al., the average maternal age in pregnancies with AEDF was found to be 31 years (8). Gestational age at AEDF diagnosis varies between studies. In the study by Müller et al., the gestational age was similarly reported as 28.5 weeks (9).

Due to the high rate of fetal distress (63.2%), our cesarean section rate was 89.4% (n=76). Similarly, a high cesarean section rate was observed in the study by Kinoshita et al., and 154 out of 167 pregnancies (92.2%) ended in cesarean section (8). The underlying reason for these high cesarean section rates is due to the sudden change in fetal well-being in AEDF cases.

In many studies of AEDF cases, birth occurs in the early preterm period. In the study of Serdaroğlu et al., the average gestational age was reported as 32.63 weeks and the birth weight as 1196.84 grams (10). In the study by Deniz and Ulker, the birth weight was around 1604 grams at approximately 29 weeks of birth (11). Our data were also consistent with these studies, the birth week was 29.74±3.85 and the average birth weight was 1031.42±485.94 grams. The reason for the variability in birth weights and birth weeks is due to the effects of conditions such as differences in clinical conditions causing AEDF and the presence of additional complications on birth weight and timing. In our study, the average time from the first detection of umbilical AEDF to birth was two days. Although the median interval from AEDF detection to delivery in our study was two days, the range was wide, from 0 to 62 days. This variation in timing is probably based on the severity of fetal compromise and maternal condition. In the study of Müller et al., the interval time was reported as 8.9 days (9). This shorter interval in our cohort likely reflects more urgent intervention due to severe fetal injury, whereas Müller's longer observation period suggests a more conservative approach allowing more time when fetal conditions permit. This difference shows that different clinical strategies can be followed to achieve the balance between placental insufficiency and the risk of premature birth.

Our perinatal loss rate was 32.9%, and two intrauterine deaths and four terminations occurred due to earlyonset FGR. On the other hand, in another study, the intrauterine death rate within 30 days was reported as 15.8% and the postnatal death rate as 11.3% (8). The reason for our high perinatal loss rate may be that our facility is a tertiary reference center.

When the pathologies accompanying AEDF cases were examined, FGR was observed in 80% of the cases, preeclampsia in 38.8%, oligohydramnios in 21.2%, and anhydramnios in 8.2%. In the study of Caradeux et al., it was reported that preeclampsia and oligohydramnios are often accompanied by early-onset FGR cases and that this is associated with placental insufficiency (4). Similarly, In the study where Wang et al. investigated high FGR rates in cases with AEDF, the researchers emphasized the association between preeclampsia and negative perinatal outcomes (12). These studies emphasize the important role of placental dysfunction in the development of complications in cases with Doppler abnormalities.

The presence of AEDF brings about serious neonatal complications due to increased preterm birth as well as intrauterine complications. In our study, neonatal complications such as ICH, RDS, sepsis, and bowel perforation were observed in cases admitted to NICU. Ertan et al. demonstrated that neonates with absent or reversed end-diastolic flow in the umbilical artery were at high risk for severe neonatal morbidities, including cerebral hemorrhage and infections (3). Similarly, Madazli et al. found that gestational age at delivery plays a crucial role in determining perinatal outcomes in growth-restricted fetuses with AEDF (13). They reported high perinatal mortality rates, particularly in those delivered before 29 weeks of gestation. The findings from both Ertan and Madazli's studies align with our observations, suggesting that AEDF and AREDF are significant predictors of poor

neonatal outcomes, necessitating timely intervention and careful perinatal management. The severity and range of complications underscore the importance of gestational age and fetal condition at the time of delivery in determining long-term neonatal health.

According to the ROC curve analysis, gestational age at birth stood out as the strongest indicator in predicting neonatal complications (AUC: 0.804). Birth weight (AUC: 0.797) and gestational age at diagnosis (AUC: 0.800) have lower predictive values. This finding emphasizes the importance of optimal birth time for neonatal outcomes. In the study of Madazli et al., it was emphasized that the timing of birth is a determining factor in perinatal outcomes, especially in AEDF cases born before the 29th week of gestation (12).

The presence of AEDF in the umbilical artery is a critical indicator of placental insufficiency and fetal risk. In the presence of AEDF, close monitoring and timely intervention are critical. Our findings highlight the importance of integrating AEDF assessment into clinical decision-making, particularly to determine the optimal timing of birth. Early identification and monitoring of AEDF allows for balancing the complications that may occur due to preterm birth against the risks of longterm intrauterine exposure that may lead to worsening of the fetal condition. This information is particularly important in cases of severe FGR, where term delivery can significantly improve neonatal outcomes.

The retrospective design of this study limits the ability to determine causality and may affect the generalizability of findings to larger populations. Data were collected from a single tertiary care center and may not reflect changes in clinical practice and patient demographics in other settings. Future studies with prospective design and multicentric collaborations are needed to confirm these findings and increase their applicability to different populations.

# Conclusions

This study highlights the critical impact of AEDF in the umbilical artery on perinatal outcomes, particularly in the context of FGR and placental insufficiency. The high rates of FGR (80%) and preeclampsia (38.8%), combined with severe neonatal complications and a significant perinatal loss rate (32.9%), emphasize the severity of the condition in pregnancies diagnosed with AEDF.

The findings of this study indicate that AEDF is a crucial predictor of poor neonatal outcomes, underscoring the need for early diagnosis and close monitoring to optimize perinatal care. As gestational age at delivery proved to be the strongest predictor of neonatal complications, careful timing of delivery is essential in balancing the risks associated with prematurity and the progression of placental insufficiency.

# **Conflict of Interest**

No conflict of interest was declared by the authors.

### Authorship Contribution

Idea/Hypothesis: NVT, GA; Design: NVT, GK; Data collection/Data processing: BTC, GA, and GK; Data Analysis: NVT, BYC; Preparation of the article: NVT, ATC

# **Financial Disclosure**

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