

Fetal Adrenal Microvascularization and Automated Three-Dimensional Adrenal Volume in Preterm Premature Rupture of Membranes: A Prospective Case–Control Study

Preterm Prematür Membran Ruptüründe Fetal Adrenal Bez Mikrovaskülarizasyonu ve Otomatik Üç Boyutlu Adrenal Hacim Ölçümü: Prospektif Bir Olgu-Kontrol Çalışması

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ABSTRACT

Aim: This study aimed to evaluate fetal adrenal gland volume and adrenal microvascularization in pregnancies complicated by preterm prelabor rupture of membranes (PPROM) and to investigate their associations with neonatal outcomes.

Materials and Methods: This prospective case-control study included 100 singleton pregnancies between 28 and 37 weeks of gestation, comprising 47 pregnancies complicated by PPRM and 53 gestational age-matched healthy controls. Fetal adrenal gland volume was measured using semi-automated three-dimensional XI-VOCAL volumetric analysis software, and adrenal gland volume corrected for estimated fetal weight was calculated. Adrenal microvascularization was assessed using two-dimensional MVFI software, and the microvascularization index (MVI) was determined. Fetal biometric measurements, Doppler ultrasonographic parameters, and neonatal outcomes were recorded for all participants. To evaluate the independent association between PPRM and adrenal gland volume, multivariable linear regression analyses were performed after adjustment for fetal growth parameters.

Results: Fetal adrenal gland volume, abdominal circumference, and estimated fetal weight were statistically significantly lower in the PPRM group than in the control group. In contrast, no statistically significant between-group differences were observed in estimated fetal weight-adjusted adrenal gland volume or MVI. In the unadjusted analysis, UA-PSV and MCA-PSV were statistically significantly lower in the PPRM group; however, after adjustment for gestational age and estimated fetal weight, only the reduction in UA-PSV remained statistically significant. No statistically significant differences were observed in the other Doppler parameters. In multivariable analyses adjusted for gestational age and fetal growth parameters, PPRM was not independently associated with adrenal gland volume. Furthermore, no statistically significant association between adrenal gland volume and the evaluated adverse neonatal outcomes was demonstrated in this sample.

Conclusion: Pregnancies complicated by PPRM are characterized by reduced fetal adrenal gland volume despite preserved adrenal microvascularization. The absence of a significant difference in estimated fetal weight-corrected adrenal gland volume suggests that the reduction in absolute adrenal gland volume is primarily attributable to impaired fetal growth rather than to PPRM itself.

Keywords: preterm premature rupture of membranes, fetal adrenal gland, XI-VOCAL, microvascularization, three-dimensional ultrasound

ÖZ

Amaç: Bu çalışmanın amacı, preterm prematür membran rüptürü (PPROM) ile komplike gebeliklerde fetal adrenal bez hacmi ve adrenal mikrovaskülarizasyonun değerlendirilmesi ile bu parametrelerin neonatal sonuçlarla ilişkisinin araştırılmasıdır.

Gereç ve Yöntem: Bu prospektif olgu-kontrol çalışmasına, gebelik haftası 28–37 arasında olan 47 PPRM olgusu ile gebelik haftası açısından eşleştirilmiş 53 sağlıklı tekil gebelik olmak üzere toplam 100 olgu dahil edildi. Fetal adrenal bez hacmi, yarı otomatik üç boyutlu XI-VOCAL hacim analiz yazılımı kullanılarak ölçüldü ve tahmini fetal ağırlığa göre düzeltilmiş adrenal bez hacmi hesaplandı. Adrenal mikrovaskülarizasyon, iki boyutlu MVFI yazılımı ile değerlendirilerek mikrovaskülarizasyon indeksi (MVI) belirlendi. Tüm olgularda fetal biyometrik ölçümler, Doppler ultrasonografi bulguları ve neonatal sonuçlar kaydedildi. PPRM ile adrenal bez hacmi arasındaki ilişkinin fetal büyümeden bağımsız olarak değerlendirilmesi amacıyla, fetal büyüme parametreleri için düzeltme yapılarak çok değişkenli doğrusal regresyon analizleri gerçekleştirildi.

Bulgular: PPRM grubunda fetal adrenal bez hacmi, abdominal çevre ve tahmini fetal ağırlık kontrol grubuna göre istatistiksel olarak anlamlı düzeyde daha düşük bulundu. Buna karşın, tahmini fetal ağırlığa göre düzeltilmiş adrenal bez hacmi ile MVI açısından gruplar arasında istatistiksel olarak anlamlı fark saptanmadı. Düzeltilmemiş analizde UA-PSV ve MCA-PSV PPRM grubunda istatistiksel olarak anlamlı düzeyde daha düşükken, gebelik haftası ve tahmini fetal ağırlık için düzeltme sonrasında yalnızca UA-PSV'deki düşüklük istatistiksel anlamlılığını korudu. Diğer Doppler parametreleri açısından gruplar arasında istatistiksel olarak anlamlı fark saptanmadı. Çok değişkenli analizlerde, gebelik haftası ve fetal büyüme parametreleri için düzeltme yapıldığında PPRM ile adrenal bez hacmi arasında bağımsız bir ilişki gösterilemedi. Bu örneklemede adrenal bez hacmi ile değerlendirilen olumsuz neonatal sonuçlar arasında istatistiksel olarak anlamlı bir ilişki gösterilemedi.

Sonuç: PPRM ile komplike gebeliklerde fetal adrenal bez hacmi azalırken adrenal mikrovaskülarizasyon korunmaktadır. Düzeltilmiş adrenal bez hacminin benzer bulunması, mutlak adrenal hacimdeki azalmanın büyük ölçüde PPRM'un doğrudan etkisinden ziyade fetal büyümenin etkilenmesine bağlı olduğunu düşündürmektedir.

Anahtar Kelimeler: preterm prematür membran rüptürü, fetal adrenal bez, XI-VOCAL, mikrovaskülarizasyon, üç boyutlu ultrasonografi

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INTRODUCTION

Preterm premature rupture of membranes (PPROM) is defined as the spontaneous rupture of the fetal membranes before 37 weeks of gestation and occurs in approximately 3–4% of all pregnancies. It accounts for a substantial proportion of spontaneous preterm births. The etiopathogenesis of PPRM is multifactorial and involves mechanisms such as inflammation, oxidative stress, extracellular matrix degradation, and cellular senescence (1, 2).

The fetal adrenal gland plays a central role in fetal growth, maturation, and stress adaptation through steroidogenesis and catecholamine secretion (3, 4). Previous studies have demonstrated that fetal adrenal gland dimensions and volumetric measurements are associated with spontaneous labor and may have predictive value for preterm delivery (5–7). However, most existing studies have focused on preterm labor or populations at high risk of preterm birth, and data specifically addressing adrenal volume changes in PPRM remain limited. Unlike preterm labor, PPRM is more frequently associated with chronic inflammation and infection, suggesting that the fetal adrenal response may differ in this condition and that alterations in the fetal stress response may contribute to its pathophysiology. A limited number of studies have reported reduced fetal adrenal medullary volume with preserved total adrenal volume in PPRM and, in contrast to findings from studies of spontaneous labor, decreased adrenal volume in pregnancies resulting in preterm birth (8, 9).

In addition, previous studies have predominantly focused on adrenal gland volume, whereas adrenal vascularization has not been evaluated in the context of PPRM. Recent advances in ultrasonography have enabled more detailed assessment of fetal organs, including adrenal volumetric and microvascular evaluation using three-dimensional imaging techniques and microvascular Doppler modalities (10, 11). Previous studies comparing two- and three-dimensional volumetric approaches have suggested that 3D techniques may provide more reliable and standardized volume assessment by allowing clearer delineation of organ boundaries (12). Given the inflammation-based pathophysiology of PPRM and the central role of the fetal adrenal gland in the fetal stress response, the combined evaluation of adrenal volume and microvascularization may provide further insight into fetoplacental stress mechanisms.

In this study, we aimed to evaluate fetal adrenal gland volume and vascularization in pregnancies complicated by PPRM and to investigate their association with perinatal outcomes. We hypothesized that PPRM is associated with a distinct pattern of adrenal development, characterized by reduced volume with relatively preserved vascularization.

MATERIALS AND METHODS

This prospective case–control study was conducted at the Perinatology Clinic of Ankara Bilkent City Hospital between November 2025 and February 2026. The study protocol was approved by the Ethics Committee of Ankara City Hospital (Approval No: E2-25-1646). Singleton pregnancies between 28+0 and 37+0 weeks of gestation diagnosed with preterm premature rupture of membranes (PPROM) were included in the study. The diagnosis of PPRM was confirmed using a PAMG-1 rapid immunoassay test. The control group consisted of gestational age–matched singleton pregnancies with intact membranes and no maternal or fetal pathology.

Inclusion criteria were defined as singleton pregnancies between 28 and 37 weeks of gestation complicated by PPRM, with diagnosis confirmed by a PAMG-1 rapid immunoassay test. Exclusion criteria included multiple pregnancy, major fetal anomalies, maternal systemic diseases, suspected chorioamnionitis at admission, and inadequate adrenal imaging quality. All ultrasonographic evaluations were performed prior to the administration of corticosteroids and antibiotics.

Clinical and obstetric data, including maternal characteristics, fetal biometric measurements, Doppler parameters, adrenal gland measurements, and neonatal outcomes, were prospectively recorded using a standardized data collection form specifically designed for the study.

Ultrasound Examination and Adrenal Volume Assessment

All ultrasonographic evaluations were performed by a single operator with more than 10 years of experience using a Samsung Hera W10 (Samsung Medison Co., Ltd., Seoul, Republic of Korea) ultrasound system equipped with a high-resolution CV1-8A transducer.

For fetal adrenal gland imaging, the adrenal gland was first visualized in real time using two-dimensional (2D) ultrasound in the axial plane. For volumetric assessment, the axial axis of the adrenal gland was used as the reference plane, and the device's semi-automated three-dimensional (3D) XI volumetric analysis algorithm was applied. The adrenal gland boundary was manually delineated on a single optimal reference image, after which the software automatically generated sequential sectional images and calculated the total adrenal gland volume (Figure 1). Corrected adrenal gland volume was calculated by dividing adrenal gland volume by estimated fetal weight and was expressed as cm³/kg.

Estimated fetal weight (EFW) was automatically calculated using the device-integrated Hadlock formula based on biparietal diameter, head circumference, abdominal circumference, and femur length measurements.

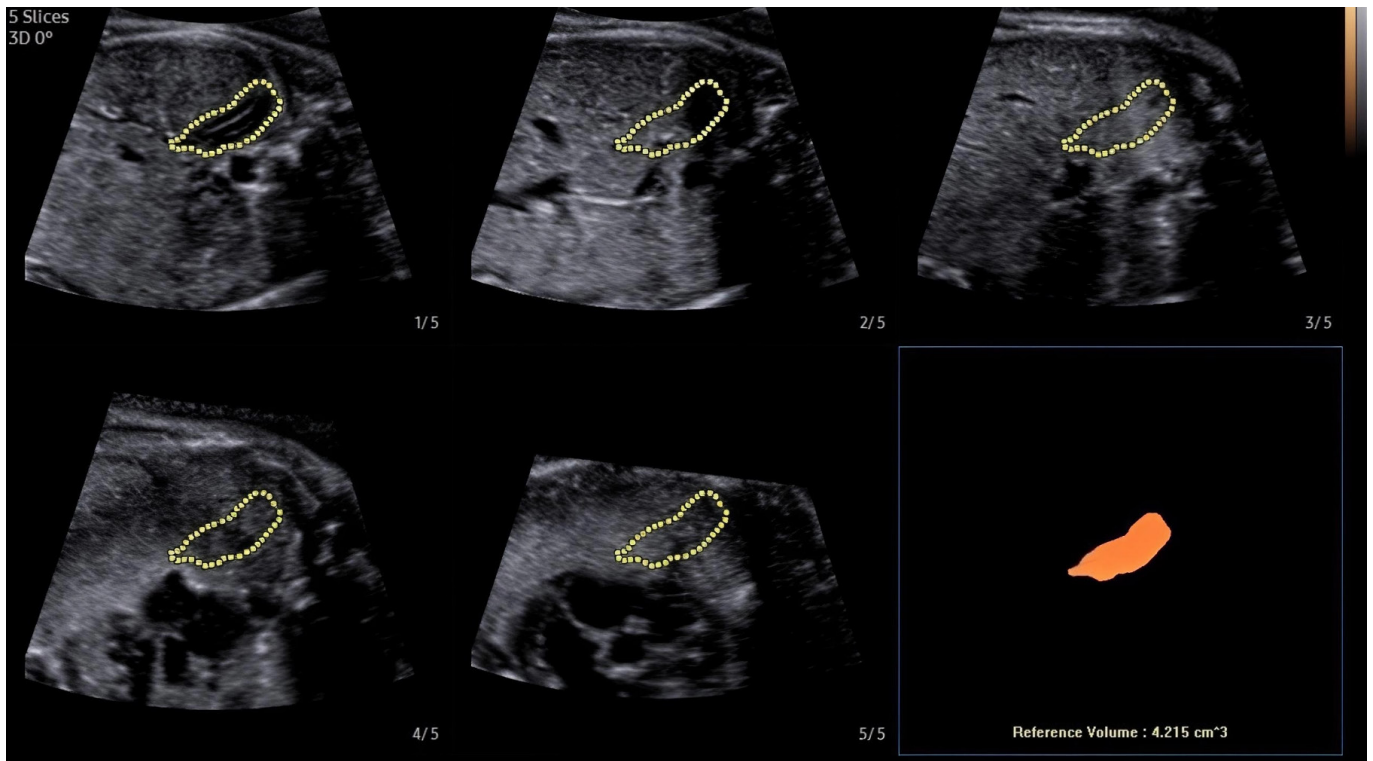


Figure 1. Three-dimensional volumetric assessment of the fetal adrenal gland using 3D XI volumetric analysis.

Microvascularization Assessment

Adrenal microvasculature was assessed using the two-dimensional microvascular imaging (MVI) mode of the ultrasound device. For

each adrenal gland, a standardized region of interest (ROI) was defined in the axial plane, and the microvascularization index (MVI) was calculated automatically (Figure 2).

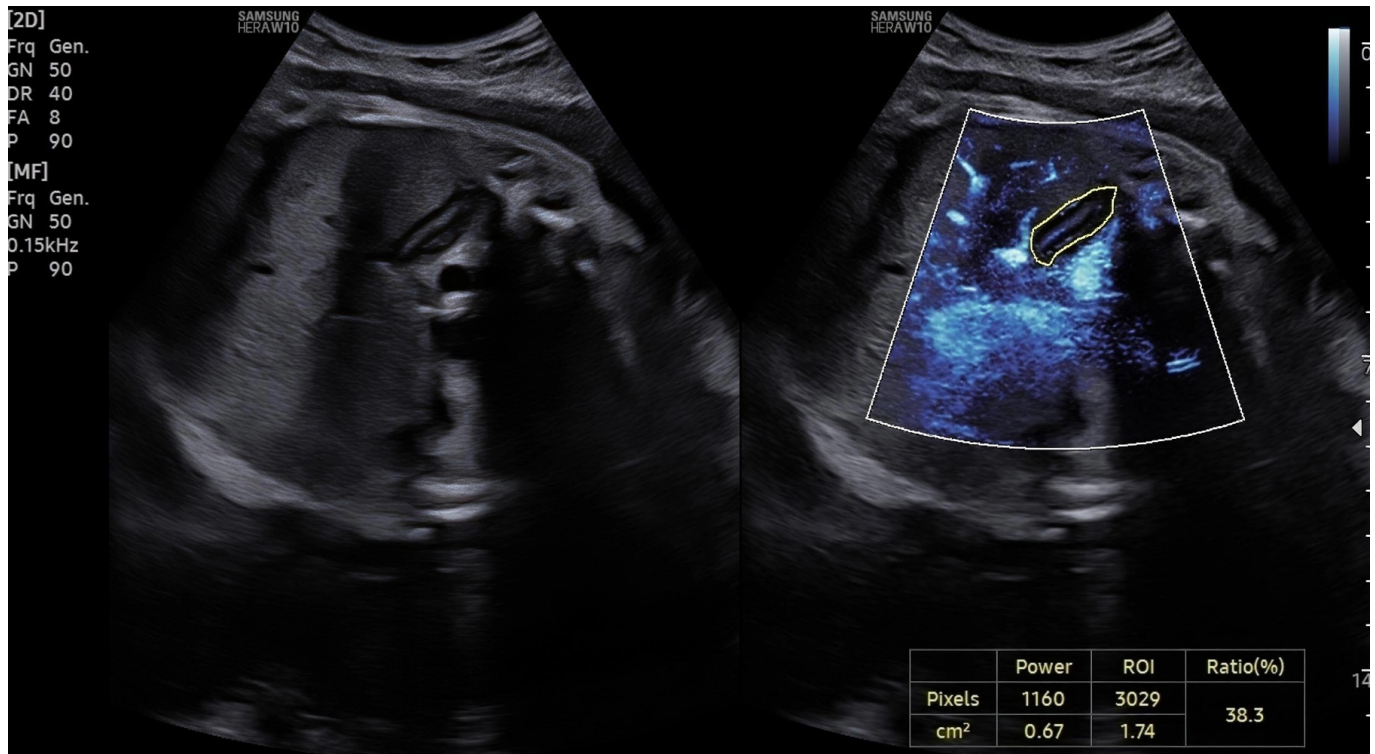


Figure 2. Assessment of fetal adrenal gland microvascularization using two-dimensional microvascular imaging.

During all examinations, gain, pulse repetition frequency, and wall filter settings were kept constant. To minimize measurement variability, all ultrasonographic assessments were performed by the same operator.

Data Collection and Neonatal Outcomes

Maternal age, gravida, parity, and body mass index were prospectively recorded. Fetal biometric measurements, estimated fetal weight, umbilical artery, middle cerebral artery, and uterine artery Doppler indices were documented.

Neonatal outcomes included gestational age at delivery, mode of delivery, birth weight, 1st- and 5th-minute Apgar scores, and neonatal intensive care unit (NICU) admission.

Statistical Analysis

Statistical analyses were performed using SPSS software (IBM SPSS Statistics for Windows, version 23.0; IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using visual and analytical methods. Normally distributed variables were expressed as mean $\pm$ standard deviation, whereas non-normally distributed variables were presented as median and interquartile range (IQR).

Comparisons between groups were performed using the independent samples t-test or Mann–Whitney U test, as appropriate. Categorical variables were compared using the Pearson chi-square test. Multivariable linear regression analyses were performed to evaluate the independent association between PPRM and adrenal gland volume after adjustment for gestational age and fetal growth parameters. A p value <0.05 was considered statistically significant.

RESULTS

A total of 100 singleton pregnancies were included in the study, comprising 53 in the control group and 47 in the PPRM group.

Table 1 summarizes the maternal, obstetric, and fetal characteristics of the study population. Maternal and obstetric characteristics were comparable between the groups. No statistically significant differences were observed in maternal age (median [IQR]: 27 [8.00] vs. 30.0 [3.75] years; $p = 0.238$), gestational age at examination (32.9 ± 2.81 vs. 31.9 ± 2.79 weeks; $p = 0.530$), gravida (median [IQR]: 2 [1.00] vs. 2 [2.00]; $p = 0.571$), parity (median [IQR]: 1 [1.00] vs. 1 [1.00]; $p = 0.512$), abortion history (median [IQR]: 0 [0.00] vs. 0 [0.00]; $p = 0.249$), or body mass index (28.40 ± 4.23 vs. 28.28 ± 4.21 kg/m²; $p = 0.960$).

Fetal biometry parameters were significantly lower in the PPRM group. Both abdominal circumference (277.6 ± 28.9 vs. 310.8 ± 23.7 mm, $p < 0.001$) and abdominal circumference percentile (41.28 ± 30.69 vs. 59.37 ± 29.24 , $p = 0.008$) were reduced. Similarly, estimated fetal weight (1849 ± 563 vs. 2664 ± 401.6 g, $p < 0.001$) and estimated fetal weight percentile (32.54 ± 25.26 vs. 52.42 ± 23.63 , $p < 0.001$) were significantly lower in the PPRM group.

Table 2 summarizes adrenal gland measurements and Doppler parameters. Adrenal gland volume was significantly lower in the PPRM group than in controls (median [IQR]: 3.17 [3.06] vs. 4.47 [2.05] cm³, $p = 0.002$). Corrected adrenal gland volume (1.83 [1.41] vs. 1.78 [0.58] cm³/kg, $p = 0.668$) and adrenal MVI (29.2 [32.50] vs. 34.4 [27.60], $p = 0.139$) did not differ significantly between groups.

In the unadjusted comparisons, umbilical artery peak systolic velocity (UA-PSV) and middle cerebral artery peak systolic velocity (MCA-PSV) were lower in the PPRM group than in controls (41.45

Table 1. Maternal and Fetal Characteristics at Examination

Variable	Control (n=53)	PPROM (n=47)	p-value
Maternal age (years)**	27 (8)	30 (3.75)	0.238
Gestational age at examination (weeks)*	32.9 ± 2.81	31.9 ± 2.79	0.530
Gravida**	2 (1)	2 (2)	0.571
Parity**	1 (1)	1 (1)	0.512
Abortions**	0 (0)	0 (0)	0.249
BMI (kg/m ²)*	28.40 ± 4.23	28.28 ± 4.21	0.960
AC (mm)*	310.8 ± 23.7	277.6 ± 28.9	<0.001
AC percentile*	59.37 ± 29.24	41.28 ± 30.69	0.008
EFW (g)*	2664 ± 401.6	1849 ± 563	<0.001
EFW percentile*	52.42 ± 23.63	32.54 ± 25.26	<0.001

*Independent samples t-test; **Mann–Whitney U test; Data are presented as mean $\pm$ SD or median (IQR); AC: abdominal circumference; EFW: estimated fetal weight

Table 2. Adrenal and Doppler Parameters

Parameter	Control (n=53)	PPROM (n=47)	p-value
Adrenal gland measurements			
Adrenal gland volume (cm ³)**	4.47 (2.05)	3.17 (3.06)	0.002
Corrected adrenal gland volume** (cm ³ /kg)	1.78 (0.58)	1.83 (1.41)	0.668
Adrenal MVI**	34.4 (27.60)	29.2 (32.50)	0.139
Doppler parameters			
UA PI*	0.88 ± 0.23	0.87 ± 0.18	0.761
UA RI*	0.58 ± 0.09	0.60 ± 0.10	0.289
UA PSV*	50.57 ± 10.49	41.45 ± 10.49	<0.001
UA S/D*	2.49 ± 0.76	2.61 ± 0.73	0.251
MCA PI*	1.80 ± 0.54	1.95 ± 0.63	0.326
MCA RI*	0.81 ± 0.10	0.83 ± 0.11	0.284
MCA PSV*	51.82 ± 12.04	43.80 ± 10.30	0.003
Uterine artery PI**	0.84 (1.23)	0.97 (0.55)	0.686
Uterine artery RI*	0.56 ± 0.23	0.62 ± 0.20	0.460
Uterine artery PSV*	65.18 ± 24.09	63.19 ± 20.88	0.930
Cerebroplacental ratio (CPR) **	1.72 (2.00)	1.69 (2.18)	0.754

*Independent samples t-test; **Mann-Whitney U test; Data are presented as mean ± SD or median (IQR); UA: umbilical artery; MCA: middle cerebral artery; Uta: uterine artery; PI: pulsatility index; RI: resistance index; PSV: peak systolic velocity; S/D: systolic/diastolic ratio

± 10.49 vs. 50.57 ± 10.49 cm/s, $p < 0.001$, and 43.80 ± 10.30 vs. 51.82 ± 12.04 cm/s, $p = 0.003$, respectively). In multivariable linear regression adjusted for gestational age and estimated fetal weight, UA-PSV remained significantly lower in the PPROM group ($B = -9.66$ cm/s, 95% CI: -15.26 to -4.06, $p = 0.001$). In contrast, the adjusted between-group difference in MCA-PSV was no longer statistically significant ($B = -1.76$ cm/s, 95% CI: -7.60 to 4.07, $p = 0.549$). No significant differences were observed in UA-PI, UA-RI, UA S/D ratio, MCA-PI, MCA-RI, uterine artery PI, uterine artery RI, uterine artery PSV, or cerebroplacental ratio (CPR) values between the groups (all $p > 0.05$).

Table 3 summarizes neonatal outcomes in the study population. Gestational age at delivery was significantly lower in the PPROM

group than in controls (33.1 ± 2.21 vs. 38.6 ± 1.18 weeks, $p < 0.001$), as was birth weight (2101 ± 543 vs. 3352 ± 364 g, $p < 0.001$). Both 1-minute and 5-minute Apgar scores were significantly lower in the PPROM group (6.24 ± 1.88 vs. 7.56 ± 0.68 , $p < 0.001$, and 7.82 ± 1.30 vs. 9.02 ± 0.49 , $p < 0.001$, respectively). Cesarean delivery and neonatal intensive care unit (NICU) admission rates were significantly higher among women with PPROM compared with controls (63.8% vs. 25.5%, $p < 0.001$, and 63.8% vs. 4.2%, $p < 0.001$, respectively).

In univariable linear regression analysis, PPROM was significantly associated with lower fetal adrenal gland volume ($B = -0.919$ cm³, 95% CI: -1.672 to -0.167, standardized $\beta = -0.248$, $p = 0.017$). However, after adjustment for gestational age and estimated fetal

Table 3. Neonatal Outcomes

Parameter	Control (n=47)	PPROM (n=47)	p-value
Gestational age at delivery (weeks)*	38.6 ± 1.18	33.1 ± 2.21	<0.001
Birth weight (g)*	3352 ± 364	2101 ± 543	<0.001
Apgar score (1st min)*	7.56 ± 0.68	6.24 ± 1.88	<0.001
Apgar score (5th min)*	9.02 ± 0.49	7.82 ± 1.30	<0.001
Cesarean delivery (%)**	25.5	63.8	<0.001
NICU admission (%)**	4.3	63.8	<0.001

* Independent samples t-test; ** Pearson chi-square test; data are presented as mean ± SD or percentage (%); NICU: neonatal intensive care unit.

weight, the association between PPRM and fetal adrenal gland volume was no longer significant ($B = -1.38$, 95% CI: -2.93 to 0.17 , $p = 0.080$), while estimated fetal weight remained an independent predictor of adrenal volume ($B < 0.001$, $p = 0.031$).

Similarly, in a model including abdominal circumference, PPRM was not associated with adrenal volume ($B = 0.023$, $p = 0.790$), whereas abdominal circumference was identified as an independent predictor ($B = 0.034$, 95% CI: 0.018 – 0.050 , $p < 0.001$).

Within the PPRM group, no statistically significant association between fetal adrenal gland volume and the evaluated neonatal outcomes was demonstrated in this sample. Adrenal volume did not differ between cases with and without delivery before 34 weeks (3.85 ± 1.89 vs. 3.89 ± 2.61 , $p = 0.607$), NICU admission (3.50 ± 1.84 vs. 4.61 ± 2.81 , $p = 0.260$), or low Apgar score (<7) (3.38 ± 1.94 vs. 4.19 ± 2.42 , $p = 0.364$).

DISCUSSION

This prospective case-control study evaluated both fetal adrenal gland volume and microvascularization in pregnancies complicated by PPRM. We found that absolute adrenal gland volume was significantly lower in the PPRM group, whereas corrected adrenal volume and adrenal microvascularization index (MVI) were comparable between groups. In addition, fetal growth parameters, including abdominal circumference and estimated fetal weight, were significantly reduced in PPRM pregnancies. Although unadjusted UA-PSV and MCA-PSV values were lower in the PPRM group, adjustment for gestational age and estimated fetal weight showed different patterns: the UA-PSV difference persisted, whereas the MCA-PSV difference was attenuated and was no longer statistically significant. Importantly, the association between PPRM and adrenal gland volume was no longer significant after adjustment for fetal growth parameters, suggesting that reduced adrenal size is primarily related to impaired fetal growth rather than PPRM itself.

Most previous studies evaluating fetal adrenal glands have focused on pregnancies at risk for spontaneous preterm birth, where adrenal enlargement has often been reported as a marker of impending labor (5, 13). However, findings in PPRM appear to differ from those observed in spontaneous preterm labor. Several studies have demonstrated reduced adrenal dimensions or altered adrenal morphology in PPRM, suggesting that chronic inflammatory exposure and prolonged membrane rupture may influence adrenal development differently from acute activation of the fetal hypothalamic-pituitary-adrenal axis associated with spontaneous

labor. Our findings of reduced adrenal volume are consistent with these observations. At the same time, the absence of differences in corrected adrenal volume and the loss of significance after adjustment indicate that fetal size is a major determinant of adrenal volume in this population (6, 9, 14).

To our knowledge, this is one of the first studies to evaluate adrenal microvascularization in PPRM using microvascular imaging technology. Although median MVI values were numerically lower in PPRM pregnancies, the difference was not statistically significant. These findings suggest that adrenal perfusion may be relatively preserved despite reductions in organ size. Adaptive fetal circulatory mechanisms are known to maintain blood flow to essential organs under conditions of intrauterine stress, and preservation of adrenal microvascularization may represent a component of this compensatory response (15). Previous studies have similarly reported relative preservation of adrenal perfusion in growth-restricted fetuses and other chronic intrauterine stress conditions (13, 14).

Doppler findings in PPRM have been inconsistent across studies. In our cohort, pulsatility and resistance indices of the umbilical, middle cerebral, and uterine arteries were comparable between groups, suggesting that global placental and fetal circulatory adaptation remained largely preserved (16, 17). Because peak systolic velocities vary with gestational age and fetal size, we adjusted the comparisons for gestational age and estimated fetal weight. The persistence of the UA-PSV difference after adjustment may indicate a PPRM-related hemodynamic alteration; however, this finding should be interpreted cautiously. Conversely, the loss of the MCA-PSV difference after adjustment suggests that the unadjusted association was largely explained by gestational age and fetal size.

The relationship between fetal adrenal measurements and neonatal outcome remains uncertain. Blue et al. reported that adrenal area did not predict neonatal morbidity among growth-restricted fetuses (18). Similarly, no statistically significant association between adrenal volume and the evaluated neonatal outcomes was demonstrated in our sample. However, these findings do not establish the predictive value of adrenal volume for short-term neonatal outcomes.

A major strength of this study is the simultaneous evaluation of adrenal volume, adrenal microvascularization, fetal growth parameters, Doppler findings, and neonatal outcomes within a prospective PPRM cohort. In addition, all examinations were performed before corticosteroid and antibiotic administration by a single experienced operator, minimizing potential measurement

variability. Because of the complex anatomy of the fetal adrenal gland, volumetric assessment can be challenging using conventional two-dimensional ultrasound. Previous studies have shown that three-dimensional techniques such as VOCAL and XI-VOCAL provide reliable and reproducible volume measurements. The use of semi-automated XI-VOCAL analysis may therefore facilitate a more standardized assessment of fetal adrenal volume in clinical practice (12, 19-22).

Several limitations should be considered. First, separate assessment of the adrenal cortex and medulla was not possible, and only total adrenal volume was evaluated. Second, the sample size may limit statistical power and generalizability. Finally, given the strong relationship between adrenal size and fetal growth, residual confounding by growth-related factors cannot be completely excluded despite multivariable adjustment. Although UA-PSV and MCA-PSV comparisons were adjusted for gestational age and estimated fetal weight, the values were not converted to gestational-age-specific multiples of the median; residual confounding therefore remains possible.

CONCLUSION

Our findings suggest that reduced adrenal gland volume in PPRM primarily reflects impaired fetal growth rather than a disease-specific adrenal adaptation. The preservation of corrected adrenal volume and microvascularization further supports this interpretation. Future studies incorporating compartment-specific adrenal assessment and larger prospective cohorts may help clarify the role of fetal adrenal changes in the pathophysiology of PPRM. These findings suggest that adrenal measurements should be interpreted in conjunction with fetal growth parameters when evaluating pregnancies complicated by PPRM.

Statement of Ethics: This prospective study was approved by the Ethics Committee of Ankara City Hospital (Approval No: E2-25-1646). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Declaration of Helsinki and its later amendments. Written informed consent was obtained from all participants prior to enrollment. Acknowledgments: The authors would like to thank all participants who contributed to this study. The authors also acknowledge the staff of the Division of Perinatology at Ankara Bilkent City Hospital for their support during data collection and clinical follow-up.

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Data Availability Statement: The data that support the findings of this study are not publicly available because of patient privacy and institutional restrictions but are available from the corresponding author upon reasonable request.

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