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Associations of first-trimester umbilical venous doppler parameters with neonatal intensive care unit admission and preterm birth: A prospective cohort study

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Abstract

Evidence regarding first-trimester umbilical venous hemodynamics and subsequent perinatal morbidity is limited. We evaluated the associations of first-trimester umbilical venous Doppler parameters with neonatal intensive care unit (NICU) admission and preterm birth in singleton pregnancies. This prospective cohort study included 90 pregnancies examined at 11+0 to 13+6 weeks. Time-averaged maximum velocity (TAMXV), umbilical vein diameter, vessel cross-sectional area, and umbilical venous blood flow (UVBF) were measured during routine first-trimester ultrasonography; pregnancy-associated plasma protein-A, free beta-human chorionic gonadotropin (free β-hCG), and nuchal translucency were also recorded. Group comparisons, logistic regression, and receiver operating characteristic analyses were performed. NICU admission occurred in 11 of 87 neonates with available outcome data, and preterm birth occurred in 10 of 90 pregnancies. First-trimester biochemical and umbilical venous Doppler parameters did not differ significantly by NICU admission or preterm birth status. In univariable analysis, higher free β-hCG multiples of the median (MoM) (odds ratio [OR], 2.64; 95% confidence interval [CI], 1.21 – 5.76; p = .015) and higher TAMXV (OR, 1.16; 95% CI, 1.00 – 1.33; p = .043) were associated with NICU admission. Neither association remained significant in the primary exploratory multivariable model. In a sensitivity analysis adjusted for gestational age at delivery, TAMXV was attenuated, whereas free β-hCG MoM remained associated with NICU admission (adjusted OR, 2.23; 95% CI, 1.03 – 4.81; p = .041). TAMXV and UVBF showed limited discrimination for NICU admission and preterm birth. No significant adjusted associations were observed between first-trimester umbilical venous Doppler parameters and either outcome. These findings are exploratory and require confirmation in larger prospective studies.

Keywords: First trimester, umbilical vein, Doppler ultrasonography, neonatal intensive care unit, preterm birth, pregnancy

Introduction

Normal placental development involves coordinated trophoblast invasion, remodeling of the uteroplacental vasculature, and progressive adaptation of the fetoplacental circulation during early gestation. Disturbances in these processes may contribute to impaired placental function and have been associated with complications such as fetal growth restriction, preeclampsia, preterm birth, intrapartum fetal compromise, and neonatal morbidity. Evaluation of early placental and fetal hemodynamics may therefore provide additional insight into physiological changes that precede clinically apparent pregnancy complications [1].

Umbilical artery Doppler ultrasonography is widely used to assess placental vascular resistance and fetal well-being, particularly in pregnancies complicated by placental insufficiency and fetal growth restriction. However, arterial Doppler findings may remain within normal ranges during the earlier stages of placental dysfunction. Assessment of other components of the fetoplacental circulation may therefore complement conventional arterial Doppler evaluation and contribute to a broader characterization of early placental and fetal adaptation [2,3].

The umbilical vein carries oxygenated and nutrient-rich blood from the placenta to the fetus. Quantitative assessment of umbilical venous circulation, including time-averaged maximum

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velocity (TAMXV), vessel diameter, vessel cross-sectional area, and umbilical venous blood flow (UVBF), may reflect aspects of placental transport capacity and fetal cardiovascular adaptation. Previous studies have reported lower UVBF measurements in pregnancies complicated by placental insufficiency and fetal growth restriction, whereas higher values have been described in association with accelerated fetal growth and large-for-gestational-age birth weight [2,4,5] .These observations suggest that umbilical venous hemodynamics may be related to placental function and fetal growth, although their clinical interpretation remains uncertain.

Most available studies have evaluated umbilical venous circulation during the second or third trimester or in pregnancies with established fetal growth abnormalities. Evidence regarding the clinical relevance of these measurements during the first trimester remains limited. In particular, it is not clear whether early variations in TAMXV and UVBF are associated with subsequent perinatal morbidity. Neonatal intensive care unit (NICU) admission is clinically relevant but may be influenced by gestational age at delivery, neonatal condition, obstetric complications, clinician judgment, and institutional practices. Preterm birth may therefore provide an additional and more consistently defined outcome when assessing the potential clinical relevance of first-trimester fetoplacental hemodynamic measurements.

Accordingly, this prospective cohort study aimed to evaluate the associations of first-trimester umbilical venous Doppler parameters, including TAMXV and UVBF, with NICU admission and preterm birth in singleton pregnancies. Given the limited evidence available in early gestation, the analyses were designed as an exploratory assessment of the relationship between first-trimester umbilical venous hemodynamics and subsequent perinatal outcomes.

Material and Methods

Study Design and Population

This prospective cohort study was conducted at a tertiary referral center affiliated with a university hospital in Türkiye. Participants were consecutively recruited beginning in November 2025, after ethics committee approval, among women with singleton pregnancies attending routine first-trimester screening between 11 + 0 and 13 + 6 weeks of gestation. Gestational age was determined using crown – rump length measured during the first-trimester ultrasound examination.

Because sufficiently comparable prospective data reporting effect estimates for first-trimester umbilical venous Doppler parameters in relation to NICU admission or preterm birth were not available at study initiation, a reliable effect size for an a priori sample size calculation could not be specified. Accordingly, the study was designed as an exploratory, hypothesis-generating prospective cohort, and all consecutively eligible women during the recruitment period were enrolled. The limited number of outcome events was recognized as a constraint on statistical precision and multivariable modeling rather than addressed using a retrospective post hoc power calculation. During the study period, 140 pregnancies were assessed for eligibility. Three pregnancies ended in missed abortion, and two pregnancies were terminated because of major fetal structural or genetic abnormalities. Follow-up and delivery data were not available at our institution for 45 pregnancies. Consequently, 90 singleton pregnancies constituted the final study cohort. NICU admission status could not be verified from the available neonatal records for three neonates. These cases were excluded only from NICU-specific analyses; no imputation was performed, and NICU analyses were conducted using the 87 neonates with available outcome data. The patient selection and follow-up process is presented in Figure 1.

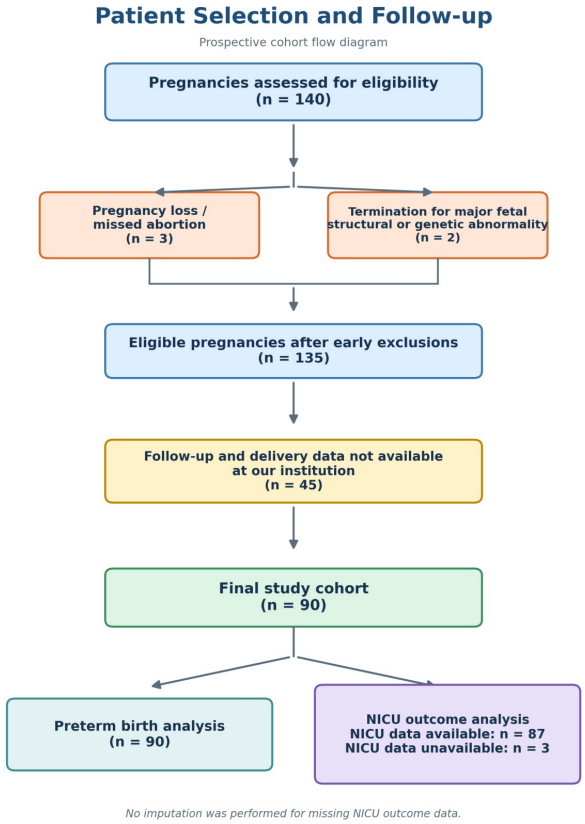

Figure 1. Flowchart of patient selection and follow-up; Of 140 pregnancies assessed, 5 were excluded because of missed abortion (n = 3) or major fetal structural/genetic abnormalities requiring termination (n = 2), and follow-up/delivery data were unavailable at our institution for 45; The final cohort comprised 90 pregnancies; NICU data were available for 87 neonates and unavailable for 3; No imputation was performed

Inclusion and Exclusion Criteria

Women were eligible for inclusion if they had a viable singleton pregnancy between 11 + 0 and 13 + 6 weeks of gestation, available first-trimester biochemical screening results, and technically adequate umbilical venous Doppler measurements.

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Pregnancies complicated by multiple gestation, major fetal structural abnormalities, known chromosomal abnormalities, congenital infections, or maternal conditions that could substantially affect placental function or fetal growth, including pregestational diabetes mellitus and chronic kidney disease, were excluded. Examinations in which adequate umbilical venous Doppler waveforms or reliable vessel diameter measurements could not be obtained were also excluded.

Ultrasound and Doppler Assessment

During routine first-trimester screening, crown – rump length (CRL) and nuchal translucency (NT) were measured. Maternal serum pregnancy-associated plasma protein-A (PAPP-A) and free beta-human chorionic gonadotropin (free β-hCG) values were obtained from the combined screening records and expressed as multiples of the median (MoM).

Umbilical venous Doppler measurements were obtained during the same examination. All ultrasound examinations and all umbilical venous Doppler measurements were performed by a single experienced perinatologist using the same Samsung V8 ultrasound system (Samsung Medison, Seoul, South Korea) according to a standardized examination protocol. The umbilical vein was identified using color Doppler, and pulsed-wave Doppler recordings were acquired from a free loop of the umbilical cord during periods without fetal movement. The insonation angle was maintained below 30° whenever technically feasible.

Time-averaged maximum velocity (TAMXV) was obtained from reproducible venous flow waveforms. Umbilical vein diameter was measured at the Doppler sampling site on magnified images, and the mean of two consecutive measurements was used in the analyses.

Vessel cross-sectional area was calculated as follows:

$$\textit{Vessel cross-sectional area} = \pi \times \textit{radius}^2$$

Umbilical venous blood flow (UVBF) was estimated using the following equation:

$$\textit{UVBF (mL/min)} =$$

$$\pi \times (\textit{umbilical vein diameter} / 2)^2 \times 0.5 \times \textit{TAMXV} \times 60$$

The coefficient of 0.5 was applied to approximate mean spatial velocity from TAMXV. Because reliable fetal weight estimation is not routinely available during the first trimester, UVBF was reported as absolute flow and was not normalized to estimated fetal weight.

Perinatal Outcome Measures

Perinatal outcome data were obtained after delivery and included birth weight, 1- and 5-minute Apgar scores, umbilical artery pH, base deficit, NICU admission, preterm birth, and neonatal mortality.

NICU admission was evaluated as the primary neonatal outcome. NICU admission was determined by the attending neonatologist according to the clinical condition of the newborn and institutional neonatal care criteria. Indications included respiratory distress requiring close monitoring or respiratory support, prematurity requiring intensive neonatal observation or supportive care, clinically significant hyperbilirubinemia requiring treatment, perinatal asphyxia or post-resuscitation monitoring, and congenital or cardiac abnormalities requiring specialized neonatal evaluation. Because NICU admission may be influenced by neonatal condition, gestational age, clinical decision-making, and institutional practices, preterm birth was additionally evaluated as a secondary outcome. Preterm birth was defined as delivery before 37 + 0 weeks of gestation. Preterm births were additionally classified as spontaneous or medically indicated. Spontaneous preterm birth was defined as preterm delivery following spontaneous onset of labor and/or preterm prelabor rupture of membranes, whereas medically indicated preterm birth referred to delivery initiated for a maternal or fetal indication. Outcome-specific analyses were performed using available cases.

Placenta-related pregnancy outcomes, including preeclampsia, fetal growth restriction, oligohydramnios, and placental abruption, were also recorded and summarized descriptively.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics software (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro – Wilk test and visual inspection of distribution plots. Normally distributed variables are presented as mean ± standard deviation, whereas non-normally distributed variables are presented as median and interquartile range. Categorical variables are reported as numbers and percentages.

Associations between continuous variables were evaluated using Pearson correlation analysis for normally distributed data and Spearman rank correlation analysis for non-normally distributed data. Correlation analyses were considered secondary and exploratory. No formal adjustment for multiple comparisons was applied; therefore, the reported P values are nominal and these findings were interpreted as hypothesis-generating rather than confirmatory. Comparisons between neonates with and without neonatal intensive care unit (NICU) admission and between preterm and term births were performed using the independent-samples t test or Mann – Whitney U test, as appropriate. Effect sizes and their 95% confidence intervals were reported where available.

Univariable binary logistic regression analyses were performed to examine the associations of maternal age, crown – rump length, free beta-human chorionic gonadotropin multiples of the median, pregnancy-associated plasma protein-A multiples of the median, nuchal translucency multiples of the median, time-averaged maximum velocity, umbilical vein diameter, vessel cross-sectional area, and umbilical venous blood flow with NICU admission and preterm birth. Results are presented as odds ratios with 95% confidence intervals.

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Exploratory multivariable binary logistic regression models included maternal age, crown – rump length, free beta-human chorionic gonadotropin multiples of the median, pregnancy-associated plasma protein-A multiples of the median, nuchal translucency multiples of the median, time-averaged maximum velocity, and umbilical venous blood flow. Umbilical vein diameter and vessel cross-sectional area were not entered into the multivariable models because of multicollinearity with the derived blood-flow measurements. Multicollinearity was assessed using variance inflation factors and tolerance values. Overall model performance was evaluated using the likelihood-ratio chi-square test and Cox – Snell R^2. Because of the limited number of outcome events, the adjusted models were considered exploratory and their estimates were interpreted cautiously. To further evaluate the potential confounding effect of gestational age at delivery on NICU admission, additional sensitivity analyses were performed using logistic regression models adjusted for gestational age at delivery. Given the limited number of NICU events, these analyses were considered exploratory.

Receiver operating characteristic curve analyses were used to assess the discriminatory ability of time-averaged maximum velocity and umbilical venous blood flow for NICU admission and preterm birth. Areas under the curve were reported with 95% confidence intervals. Outcome-specific analyses were based on cases with available data. All tests were two-sided, and $p < .05$ was considered statistically significant.

Ethical Approval

The study protocol was approved by the Göztepe Prof. Dr. Süleyman Yalçın City Hospital non-interventional clinical research ethics committee of the participating tertiary referral center (approval no. 2025/0265; November 6, 2025). Written informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Study Population and Descriptive Findings

A total of 90 singleton pregnancies were included in the study. Maternal age was available for 89 participants, with a mean of 29.57 ± 5.25 years. The mean crown – rump length (CRL) was 60.73 ± 7.42 mm. Mean first-trimester free beta-human chorionic gonadotropin (free β-hCG) and pregnancy-associated plasma protein-A (PAPP-A) levels were 1.10 ± 0.72 and 1.20 ± 0.54 multiples of the median (MoM), respectively. The mean nuchal translucency (NT) MoM was 1.08 ± 0.21.

The mean time-averaged maximum velocity (TAMXV) was 12.42 ± 3.61 cm/s, the mean umbilical vein diameter was 0.12 ± 0.02 cm, and the mean umbilical venous blood flow (UVBF) was 4.62 ± 2.00 mL/min. The mean birth weight was 3232.46 ± 468.51 g. Mean 1- and 5-minute Apgar scores were 7.33 ± 1.11 and 8.84 ± 0.91, respectively. The mean umbilical artery pH was 7.31 ± 0.09, and the mean base deficit was 5.02 ± 3.29. The demographic, biochemical, Doppler, and neonatal characteristics of the study population are presented in Table 1.

Table 1. Demographic, biochemical, doppler, and neonatal characteristics of the study population

Variable	N	Value
Maternal age, years	89	29.57 ± 5.25
Crown – rump length, mm	90	60.73 ± 7.42
Free β-hCG, MoM	90	1.10 ± 0.72
PAPP-A, MoM	90	1.20 ± 0.54
Nuchal translucency, MoM	90	1.08 ± 0.21
TAMXV, cm/s	90	12.42 ± 3.61
Umbilical vein diameter, cm	90	0.12 ± 0.02
Vessel cross-sectional area, cm²	90	0.01 ± 0.00
UVBF, mL/min	90	4.62 ± 2.00
Birth weight, g	90	3232.46 ± 468.51
1-minute Apgar score	90	7.33 ± 1.11
5-minute Apgar score	90	8.84 ± 0.91
Umbilical artery pH	90	7.31 ± 0.09
Base deficit	90	5.02 ± 3.29
Preterm birth, n/N (%)	90	10/90 (11.1)
NICU admission, n/N (%)	87	11/87 (12.6)
Neonatal death, n/N (%)	90	0/90 (0.0)

Data are presented as mean ± standard deviation unless otherwise indicated; NICU admission data were available for 87 neonates; three records were missing; β-hCG: beta-human chorionic gonadotropin, MoM: multiples of the median, NICU: neonatal intensive care unit, PAPP-A: pregnancy-associated plasma protein-A, TAMXV: time-averaged maximum velocity, UVBF: umbilical venous blood flow.

NICU admission status was available for 87 neonates. Eleven neonates were admitted to the NICU, whereas 76 did not require NICU admission; data were unavailable for 3 neonates. Among the 11 neonates admitted to the NICU, the most frequent indication for admission was transient tachypnea of the newborn (TTN) (n = 9, 81.8%). One neonate was admitted because of clinically significant hyperbilirubinemia (n = 1, 9.1%), and one had multiple indications, including prematurity, TTN, and suspected perinatal asphyxia (n = 1, 9.1%). Preterm birth occurred in 10 pregnancies, whereas 80 pregnancies resulted in term delivery. All 10 preterm births were spontaneous; no medically indicated preterm births occurred in the study cohort. No neonatal deaths were observed. Preeclampsia occurred in 3 pregnancies (3.3%), fetal growth restriction in 7 (7.8%), oligohydramnios in 2 (2.2%), and placental abruption in 1 (1.1%). Given the small number of events, these placenta-related outcomes were evaluated descriptively.

Correlation Analyses

Exploratory correlations among the maternal, biochemical, and umbilical venous Doppler measurements are presented in

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Supplementary Table 1. CRL showed positive correlations with free β-hCG MoM (r = 0.220, p = .037), NT MoM (r = 0.265, p = .012), umbilical vein diameter (r = 0.351, p < .001), vessel cross-sectional area (r = 0.268, p = .011), and UVBF (r = 0.306, p = .003). Free β-hCG MoM was positively correlated with PAPP-A MoM (r = 0.369, p < .001). TAMXV was positively correlated with UVBF (r = 0.623, p < .001). Umbilical vein diameter and vessel cross-sectional area were also positively correlated with UVBF (r = 0.761 and r = 0.771, respectively; both p < .001).

Correlations between the evaluated first-trimester parameters and neonatal measurements are presented in Table 2. NT MoM showed a weak positive correlation with birth weight (r = 0.249, p = .018). TAMXV showed a weak negative correlation with the 5-minute Apgar score (r = -0.292, p = .005), while UVBF showed a weak negative correlation with base deficit (r = -0.212, p = .045). No other statistically significant correlations were observed between the evaluated first-trimester parameters and neonatal measurements.

Table 2. Correlations between first-trimester parameters and neonatal outcomes

Variable	Birth weight	Apgar 1 min	Apgar 5 min	Umbilical artery pH	Base deficit
Maternal age	-0.011 (.919)	0.085 (.429)	0.130 (.226)	0.021 (.847)	-0.086 (.423)
CRL	0.139 (.190)	0.084 (.429)	0.076 (.479)	0.161 (.130)	-0.184 (.082)
Free β-hCG, MoM	0.027 (.797)	-0.044 (.683)	-0.016 (.878)	-0.025 (.816)	0.052 (.627)
PAPP-A, MoM	0.150 (.158)	-0.070 (.512)	0.074 (.490)	0.028 (.794)	0.052 (.629)
NT, MoM	**0.249 (.018)**	0.006 (.954)	-0.092 (.388)	0.043 (.691)	0.097 (.364)
TAMXV	0.049 (.648)	-0.121 (.257)	**-0.292 (.005)**	-0.056 (.601)	-0.037 (.732)
UV diameter	0.116 (.276)	0.142 (.181)	0.026 (.810)	0.185 (.081)	-0.175 (.100)
Vessel area	0.072 (.498)	0.143 (.178)	0.026 (.810)	0.185 (.081)	-0.175 (.100)
UVBF	0.075 (.480)	0.093 (.383)	-0.110 (.301)	0.128 (.230)	**-0.212 (.045)**

Values are correlation coefficient r (P value); Bold values indicate P < .05; Pearson or Spearman correlation analysis was used, as appropriate; β-hCG: beta-human chorionic gonadotropin, CRL: crown-rump length, MoM: multiples of the median, NT: nuchal translucency, PAPP-A: pregnancy-associated plasma protein-A, TAMXV: time-averaged maximum velocity, UV: umbilical vein, UVBF: umbilical venous blood flow

Group Comparisons According to NICU Admission and Preterm Birth

Comparisons according to NICU admission and preterm birth status are presented in Table 3. In Panel A, no statistically significant differences were observed between neonates with and without NICU admission in terms of CRL, PAPP-A MoM, NT MoM, umbilical vein diameter, vessel cross-sectional area, TAMXV, or UVBF. Free β-hCG MoM was numerically higher among neonates admitted to the NICU than among those who were not admitted [1.14 (0.84 – 2.33) vs. 0.88 (0.62 – 1.31)], although the difference did not reach statistical significance (p = .055).

In Panel B, no statistically significant differences were observed between the 10 preterm and 80 term pregnancies in terms of CRL, free β-hCG MoM, PAPP-A MoM, NT MoM, umbilical vein diameter, vessel cross-sectional area, TAMXV, or UVBF.

Logistic Regression Analyses

The univariable and exploratory multivariable logistic regression analyses for NICU admission and preterm birth are presented in Table 4.

In the NICU admission analyses shown in Panel A, free β-hCG MoM was associated with NICU admission in the univariable model (odds ratio [OR], 2.64; 95% confidence interval [CI], 1.21 – 5.76; p = .015). TAMXV was also associated with NICU admission in the univariable analysis (OR, 1.16; 95% CI, 1.00 – 1.33; p = .043). However, neither free β-hCG MoM nor TAMXV remained statistically significant in the exploratory multivariable model (adjusted OR, 2.45; 95% CI, 0.98 – 6.11; p = .054 and adjusted OR, 1.30; 95% CI, 0.99 – 1.71; p = .058, respectively). The overall multivariable model did not reach statistical significance (model $\chi^2(7) = 12.5$, p = .084; Cox – Snell $R^2 = 0.14$).

In additional sensitivity analyses adjusted for gestational age at delivery, TAMXV was no longer significantly associated with NICU admission (adjusted OR, 1.13; 95% CI, 0.98 – 1.31; p = .091). In contrast, free β-hCG MoM remained significantly associated with NICU admission (adjusted OR, 2.23; 95% CI, 1.03 – 4.81; p = .041). No statistically significant associations were observed for the other evaluated parameters. The complete results are presented in Supplementary Table 2.

In the preterm birth analyses shown in Panel B, none of the evaluated variables demonstrated a statistically significant association with preterm birth in either the univariable or exploratory multivariable models. The overall multivariable model was not statistically significant (model $\chi^2(7) = 4.58$, p = .711; Cox – Snell $R^2 = 0.05$).

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Table 3. Comparisons of first-trimester parameters according to NICU admission and preterm birth

Panel A. NICU admission				
Variable	**NICU admission (n = 11)**	**No NICU admission (n = 76)**	**p**	**Effect size (95% CI)**
CRL, mm	61.73 ± 6.59	60.49 ± 7.66	.612	0.16 (-0.47 to 0.80)
PAPP-A, MoM	1.14 ± 0.49	1.22 ± 0.55	.641	0.15 (-0.48 to 0.78)
NT, MoM	1.12 ± 0.14	1.07 ± 0.21	.508	0.21 (-0.42 to 0.85)
UV diameter, cm	0.12 ± 0.02	0.13 ± 0.02	.181	0.44 (-0.20 to 1.07)
UVBF, mL/min	4.94 ± 2.75	4.61 ± 1.92	.614	0.16 (-0.47 to 0.80)
Free β-hCG, MoM†	1.14 (0.84 – 2.33)	0.88 (0.62 – 1.31)	.055	0.36 (0.16 to 0.53)
TAMXV, cm/s†	12.6 (10.8 – 16.6)	11.6 (10.3 – 13.0)	.170	0.26 (0.05 to 0.45)
Vessel area, cm²†	0.01 (0.01 – 0.01)	0.01 (0.01 – 0.02)	.163	0.26 (0.05 to 0.45)
Panel B. Preterm birth				
Variable	**Preterm (n = 10)**	**Term (n = 80)**	**p**	**Effect size (95% CI)**
CRL, mm	62.73 ± 7.28	60.48 ± 7.45	.370	0.30 (-0.36 to 0.96)
PAPP-A, MoM	1.11 ± 0.55	1.21 ± 0.54	.596	0.18 (-0.48 to 0.84)
NT, MoM	1.05 ± 0.16	1.08 ± 0.21	.702	0.13 (-0.53 to 0.79)
UV diameter, cm	0.13 ± 0.03	0.12 ± 0.02	.263	0.38 (-0.28 to 1.04)
UVBF, mL/min	5.56 ± 3.08	4.51 ± 1.82	.318	0.53 (-0.14 to 1.19)
Free β-hCG, MoM†	0.84 (0.46 – 2.08)	0.90 (0.65 – 1.35)	.705	0.07 (-0.14 to 0.27)
TAMXV, cm/s†	11.8 (10.7 – 14.3)	11.6 (10.3 – 13.3)	.546	0.12 (-0.09 to 0.32)
Vessel area, cm²†	0.01 (0.01 – 0.02)	0.01 (0.01 – 0.01)	.465	0.14 (-0.07 to 0.34)

Data are presented as mean ± standard deviation, except variables marked with †, which are presented as median (interquartile range); Independent-samples t test or Mann-Whitney U test was used, as appropriate; Effect size is reported as Cohen d for normally distributed variables and r for non-normally distributed variables; β-hCG: beta-human chorionic gonadotropin, CI: confidence interval, CRL: crown-rump length, MoM: multiples of the median, NICU: neonatal intensive care unit, NT: nuchal translucency, PAPP-A: pregnancy-associated plasma protein-A, TAMXV: time-averaged maximum velocity, UV: umbilical vein, UVBF: umbilical venous blood flow

Table 4. Logistic regression analyses for NICU admission and preterm birth

Variable	**Univariable OR (95% CI)**	**P**	**Adjusted OR (95% CI)**	**Adjusted P**
Panel A. NICU admission				
Maternal age, per year	1.05 (0.93 – 1.20)	.416	1.09 (0.94 – 1.27)	.265
CRL, per mm	1.02 (0.94 – 1.11)	.607	1.00 (0.90 – 1.12)	.952
Free β-hCG, per 1 MoM	2.64 (1.21 – 5.76)	.015	2.45 (0.98 – 6.11)	.054
PAPP-A, per 1 MoM	0.74 (0.21 – 2.56)	.637	0.78 (0.16 – 3.86)	.756
NT, per 1 MoM	2.95 (0.12 – 69.96)	.504	7.64 (0.16 – 370.30)	.304
TAMXV, per 1 cm/s	1.16 (1.00 – 1.33)	.043	1.30 (0.99 – 1.71)	.058
UVBF, per 1 mL/min	1.08 (0.80 – 1.45)	.610	0.77 (0.44 – 1.34)	.358
Panel B. Preterm birth				
Maternal age, per year	0.99 (0.87 – 1.13)	.911	0.99 (0.86 – 1.13)	.195
CRL, per mm	1.04 (0.95 – 1.14)	.368	1.04 (0.94 – 1.16)	.402
Free β-hCG, per 1 MoM	1.18 (0.50 – 2.79)	.697	1.47 (0.53 – 4.04)	.257
PAPP-A, per 1 MoM	0.70 (0.19 – 2.55)	.592	0.36 (0.07 – 1.95)	.179
NT, per 1 MoM	0.53 (0.02 – 13.26)	.699	0.17 (0.01 – 8.02)	.800
TAMXV, per 1 cm/s	1.06 (0.91 – 1.24)	.431	0.91 (0.72 – 1.16)	.208
UVBF, per 1 mL/min	1.25 (0.94 – 1.67)	.127	1.40 (0.91 – 2.15)	.725

Panel A: reference category, no NICU admission; Cox-Snell $R^2 = 0.14$; model chi-square(7) = 12.5, p = .084; Panel B: reference category, term birth; Cox-Snell $R^2 = 0.05$; model chi-square(7) = 4.58, p = .711; Umbilical vein diameter and vessel cross-sectional area were omitted because they produced unstable univariable estimates and were not entered into the adjusted models because of multicollinearity. Adjusted models were considered exploratory because of the limited number of outcome events; beta-hCG: beta-human chorionic gonadotropin, CI: confidence interval, CRL: crown-rump length, MoM: multiples of the median, NICU: neonatal intensive care unit, NT: nuchal translucency, OR: odds ratio, PAPP-A: pregnancy-associated plasma protein-A, TAMXV: time-averaged maximum velocity, UVBF: umbilical venous blood flow

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Receiver Operating Characteristic Analyses

The receiver operating characteristic analyses of TAMXV and UVBF for NICU admission and preterm birth are summarized in Table 5 and illustrated in Figure 2.

For NICU admission, the area under the curve was 0.63 (95% CI, 0.44 – 0.82; p = .170) for TAMXV and 0.51 (95% CI, 0.30 – 0.72; p = .929) for UVBF. For preterm birth, the area under the curve was 0.56 (95% CI, 0.37 – 0.75; p = .546) for TAMXV and 0.58 (95% CI, 0.39 – 0.77; p = .400) for UVBF. These analyses did not demonstrate statistically significant discriminatory performance, and cutoff values were therefore not derived.

Table 5. Receiver operating characteristic analyses of TAMXV and UVBF for NICU admission and preterm birth

Outcome	Parameter	AUC	95% CI	Standard error	p
NICU admission	TAMXV	0.63	0.44 – 0.82	0.10	.170
NICU admission	UVBF	0.51	0.30 – 0.72	0.11	.929
Preterm birth	TAMXV	0.56	0.37 – 0.75	0.10	.546
Preterm birth	UVBF	0.58	0.39 – 0.77	0.10	.400

No ROC analysis reached statistical significance; therefore, cutoff values were not derived; AUC: area under the curve, CI: confidence interval, NICU: neonatal intensive care unit, TAMXV: time-averaged maximum velocity, UVBF: umbilical venous blood flow

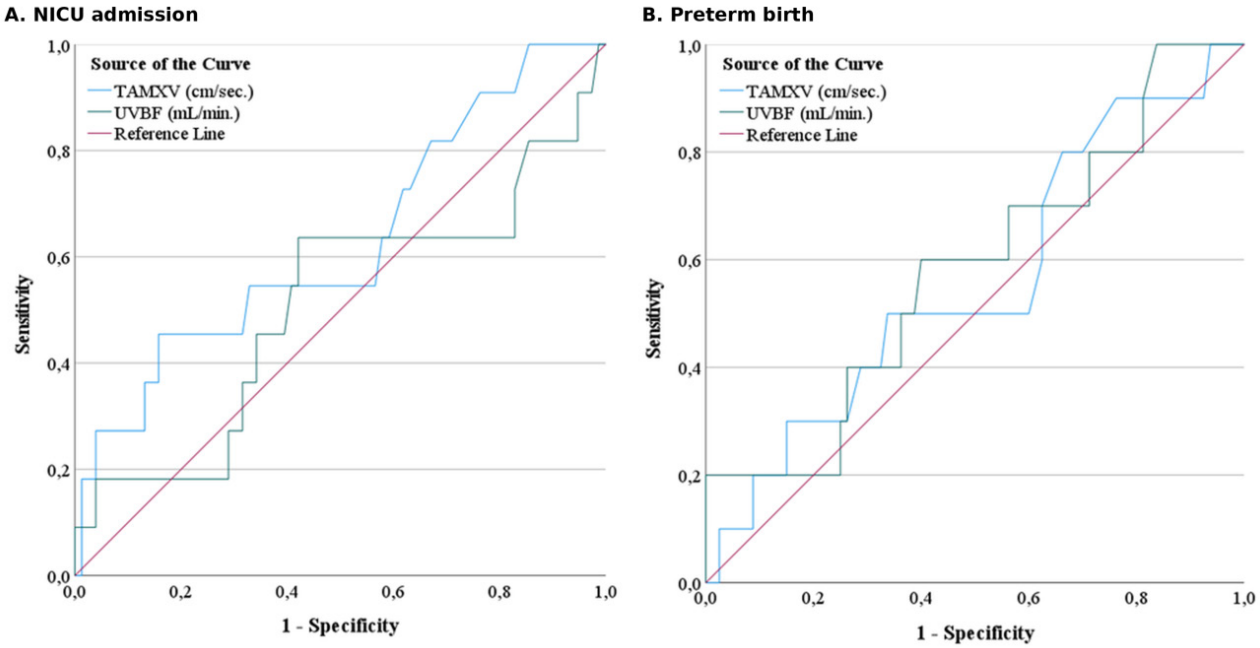

Figure 2. Receiver operating characteristic curves of time-averaged maximum velocity and umbilical venous blood flow for neonatal intensive care unit admission (A) and preterm birth (B); NICU: neonatal intensive care unit, ROC: receiver operating characteristic, TAMXV: time-averaged maximum velocity, UVBF: umbilical venous blood flow

Discussion

This prospective cohort study explored the associations of first-trimester umbilical venous Doppler parameters with NICU admission and preterm birth in singleton pregnancies. Group comparisons did not identify statistically significant differences in the evaluated biochemical or umbilical venous Doppler measurements according to NICU admission or preterm birth status. In the univariable analyses, higher free β-hCG MoM and TAMXV were associated with NICU admission. However, neither association remained statistically significant in the primary exploratory multivariable model, and the overall model was not statistically significant. In addition, TAMXV and UVBF showed limited discriminatory performance for both NICU admission and preterm birth. Taken together, the findings do not provide evidence that isolated first-trimester umbilical venous measurements can reliably identify pregnancies at risk of these outcomes.

Umbilical venous blood flow is an important component of fetoplacental circulation and may reflect placental transport capacity, fetal metabolic requirements, and fetal cardiovascular

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adaptation [6]. Impaired placental development may alter these processes and has been associated with fetal growth restriction and other placenta-related complications [1,2]. Previous studies have predominantly evaluated umbilical venous circulation in pregnancies complicated by fetal growth abnormalities or established placental dysfunction. Reduced umbilical venous flow has been reported in growth-restricted fetuses [1,3,5], whereas higher first-trimester flow measurements have been associated with large-for-gestational-age birth weight [4]. These findings suggest that umbilical venous hemodynamics may be more informative in populations with established or evolving placental dysfunction than in an unselected first-trimester cohort.

Maternal cardiovascular and fetal growth characteristics may also influence umbilical venous circulation. Previous studies have demonstrated relationships between umbilical venous flow, maternal hemodynamics, fetal growth restriction, and gestational diabetes [7-9]. First-trimester measurement of umbilical venous flow has been shown to be technically feasible [10], and fetal hemodynamic patterns may vary according to fetal growth characteristics [11]. However, technical feasibility does not necessarily translate into clinical discrimination for later adverse outcomes. In the present cohort, the positive correlations between CRL, umbilical vein dimensions, and UVBF suggest that these measurements may partly reflect physiological fetal growth and maturation of the fetoplacental circulation.

Exploratory analyses identified weak correlations between NT MoM and birth weight, between TAMXV and the 5-minute Apgar score, and between UVBF and base deficit. These findings should be interpreted cautiously because the correlations were modest, several statistical comparisons were performed, and no adjustment for multiple testing was applied. In addition, the observed correlations do not establish a causal relationship or indicate that these measurements have sufficient clinical value for individual risk assessment.

NICU admission is clinically relevant but represents a heterogeneous outcome. The decision to admit a neonate may be influenced by gestational age, birth weight, respiratory status, delivery circumstances, neonatal adaptation, clinician judgment, and institutional practices. A first-trimester Doppler measurement would therefore be unlikely to capture all factors contributing to subsequent NICU admission. Preterm birth was also evaluated because it provides a more consistently defined perinatal outcome. Nevertheless, no statistically significant group differences, regression associations, or discriminatory performance were identified for preterm birth in the present cohort.

Free β-hCG MoM and TAMXV were associated with NICU admission in the univariable logistic regression analyses, despite the absence of statistically significant differences in the corresponding group comparisons. Group comparisons and regression analyses assess related but different statistical contrasts, and their results may diverge, particularly when the outcome group is small. In the primary exploratory multivariable model, neither association remained statistically significant. In the sensitivity analysis adjusted for gestational age at delivery, the association between TAMXV and NICU admission was attenuated and was no longer statistically significant, whereas free β-hCG MoM remained significantly associated with NICU admission. Given the limited number of NICU events, this finding should be considered hypothesis-generating and interpreted cautiously.

The ROC analyses further indicated that TAMXV and UVBF had limited ability to distinguish pregnancies according to subsequent NICU admission or preterm birth. The wide confidence intervals around the area-under-the-curve estimates also suggest considerable uncertainty. Therefore, these ROC findings should be regarded as exploratory and should not be interpreted as evidence of diagnostic or predictive utility. Accordingly, the present findings do not support the use of first-trimester TAMXV or UVBF as stand-alone screening measures for these outcomes. Future studies may obtain more clinically relevant information by combining serial umbilical venous measurements with maternal characteristics, placental biomarkers, arterial Doppler parameters, and standardized placenta-related outcomes.

Strengths and Limitations

The strengths of this study include its prospective cohort design, standardized first-trimester ultrasound protocol, assessment of several components of umbilical venous circulation, and follow-up of the pregnancies until delivery. The ultrasound examinations and all umbilical venous Doppler measurements were performed by a single experienced perinatologist using the same ultrasound system and a standardized examination protocol. The inclusion of group comparisons, regression analyses, and ROC analyses also allowed the findings to be evaluated using complementary statistical approaches.

Several limitations should be considered. First, the cohort was relatively small, and only 11 NICU admissions and 10 preterm births occurred. The limited number of events reduced statistical precision and constrained the stability of the multivariable models. The adjusted analyses should therefore be regarded as exploratory, particularly because several predictors were evaluated relative to the number of outcome events. Second, the single-center design may limit the generalizability of the findings, especially because NICU admission practices may vary among institutions. Third, NICU admission data were unavailable for three neonates.

Fourth, formal intraobserver reproducibility was not prospectively assessed; therefore, intraclass correlation coefficient (ICC) data were unavailable Interobserver reproducibility could not be evaluated because all Doppler measurements were performed by a single operator.

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Fifth, only first-trimester measurements were assessed. Serial evaluation during the second and third trimesters might have provided additional information regarding changes in fetoplacental circulation over time. Sixth, NICU admission is influenced by several prenatal, intrapartum, neonatal, and institutional factors that were not fully represented in the statistical models. Although placenta-related pregnancy outcomes were reviewed separately, the small number of events precluded reliable inferential or regression analyses for these outcomes. Finally, the exploratory correlation analyses involved multiple comparisons, which may have increased the possibility of chance findings.

Conclusion

In this sample, no statistically significant adjusted association was demonstrated between first-trimester TAMXV or UVBF and subsequent NICU admission or preterm birth. Although free β-hCG MoM and TAMXV were associated with NICU admission in univariable analyses, neither remained significant in the primary exploratory multivariable model. In a sensitivity analysis adjusted for gestational age at delivery, the association with TAMXV was attenuated, whereas free β-hCG MoM remained statistically significant. Given the limited number of outcome events, these findings should be regarded as hypothesis-generating. Larger, adequately powered prospective studies incorporating serial measurements and standardized placenta-related outcomes are required.

Ethical Approval

The study protocol was approved by the Göztepe Prof. Dr. Süleyman Yalçin City Hospital non-interventional clinical research ethics committee of the participating tertiary referral center (approval no. 2025/0265; November 6, 2025).

Patient Consent

Written informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Conflict of Interest

The authors confirm the absence of any conflicts associated with this work.

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References

1. Rigano S, Bozzo M, Ferrazzi E, et al. Early and persistent reduction in umbilical vein blood flow in the growth-restricted fetus: a longitudinal study. Am J Obstet Gynecol. 2001;185:834-8.
2. Figueras F, Gratacós E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. Fetal Diagn Ther. 2014;36:86-98.
3. Rizzo G, Capponi A, Pietrolucci ME, et al. First-trimester umbilical vein blood flow in pregnancies with low serum pregnancy-associated plasma protein-A levels: an early predictor of fetal growth restriction. Ultrasound Obstet Gynecol. 2010;36:433-8.
4. Rizzo G, Mappa I, Bitsadze V, et al. Role of first-trimester umbilical vein blood flow in predicting large-for-gestational-age at birth. Ultrasound Obstet Gynecol. 2020;56:67-72.
5. Hamidi OP, Driver C, Steller JG, et al. Umbilical venous volume flow in late-onset fetal growth restriction. J Ultrasound Med. 2023;42:173-83. Correction in: J Ultrasound Med. 2024;43:2009.
6. Barbieri M, Denis Di Martino D, et al. Umbilical vein blood flow: state-of-the-art. J Clin Ultrasound. 2023;51:318-25.
7. Valensise H, Farsetti D, Pometti F, et al. The cardiac-fetal-placental unit: fetal umbilical vein flow rate is linked to the maternal cardiac profile in fetal growth restriction. Am J Obstet Gynecol. 2023;228:222.e1-12.
8. Farsetti D, Pometti F, Tiralongo GM, et al. Distinction between SGA and FGR by means of fetal umbilical vein flow and maternal hemodynamics. J Matern Fetal Neonatal Med. 2022;35:6593-9.
9. Farsetti D, Nardini S, Maffi L, et al. Umbilical venous flow and maternal hemodynamics as predictors of impaired fetal growth in gestational diabetes: a prospective study. J Perinat Med. 2026;54:51-60.
10. Rizzo G, Capponi A, Pietrolucci ME, Arduini D. Umbilical vein blood flow at 11+0 to 13+6 weeks of gestation. J Matern Fetal Neonatal Med. 2010;23:315-9.
11. Ebbing C, Rasmussen S, Kiserud T. Fetal hemodynamic development in macrosomic growth. Ultrasound Obstet Gynecol. 2011;38:303-8.