Accurate prediction of growth-restricted neonates at term using machine learning

Key words: adverse perinatal; artificial intelligence; cerebroplacental ratio; Doppler; estimated fetal weight; fetal biometry; growth restriction; machine learning; outcomes; small-for-gestational age; third-trimester ultrasound scan; uterine artery

OBJECTIVE: Growth-restricted neonates are at risk of short and long-term adverse outcomes.[1] Accurate prenatal identification of at-risk fetuses is critical to improving these outcomes. False positives can lead to unnecessary interventions and increased healthcare costs, while missed cases increase the risk of perinatal morbidity and mortality. Machine learning can enhance the predictive accuracy of various health-related outcomes. This study uses late third-trimester scan data to evaluate a novel machine learning algorithm to improve predictive accuracy at term.

STUDY DESIGN: This cohort study retrospectively analyzed data from singleton pregnancies that underwent routine third-trimester ultrasound scans between 35^{+0} and 37^{+6} weeks of gestation. Pregnancies with significant structural or genetic abnormalities or incomplete outcome data were excluded. Maternal demographic characteristics, extracted from hospital electronic records, included maternal age, ethnicity, nulliparity, previous stillbirth, body mass index, smoking or alcohol consumption, mode of conception, and the development of gestational diabetes or hypertensive disorders of pregnancy. The routine ultrasound scans measured the fetal head circumference, abdominal circumference (AC), femur length, the pulsatility index of the umbilical artery, middle cerebral artery, uterine artery Doppler and cerebroplacental ratio (CPR). Fetal biometry was evaluated following the International Society of Ultrasound in Obstetrics and Gynecology guidelines[2], and the estimated fetal weight (EFW) was calculated. AC, EFW, Doppler parameters, and neonatal birthweight were adjusted for gestational age by converting them into centiles.[3–6] Logistic regression and Random Forest machine learning models were developed to predict the study outcome: a growth-restricted neonate, defined as either a birthweight <third centile or a birthweight between the third and 10th centiles with adverse outcomes, including intrauterine death, neonatal death, or neonatal intensive care unit admission for at least 48 hours. Model performance was assessed using the Area Under the Receiver Operating Characteristic Curve (AUROC), sensitivity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratios, and feature importance.

RESULTS: The study included 14,917 pregnancies, with a median gestational age of 36^{+0} weeks at an ultrasound scan. There were 182 (1.2%) growth-restricted neonates. The demographic and clinical characteristics of patients with and without a growth-restricted neonate as well as the variables included in the prediction models are presented in Supplementary Tables 1 and 2. For the prediction of a growth-restricted neonate, at a false positive rate of 10%, the machine learning model had an AUROC of 0.94, sensitivity 81%, PPV 89%, and NPV 82% compared to 0.95, 83%, 89%, and 84%, respectively for the traditional logistic regression model (Table 1). Feature importance analysis revealed that the EFW centile was the most influential variable in the model. After

TABLE 1
Evaluating the predictive performance for growth-restricted neonates

Performance metrics	Logistic regression	Random Forest
Area under the receiver operator curve (AUROC)	0.945 (0.941–0.950)	0.940 (0.936–0.946)
Sensitivity		
10% FPR	83%	81%
15% FPR	88%	90%
20% FPR	93%	93%
Positive predictive value		
10% FPR	89%	89%
15% FPR	85%	85%
20% FPR	82%	82%
Negative predictive value		
10% FPR	84%	82%
15% FPR	88%	89%
20% FPR	92%	92%
Likelihood ratio (-, +)		
10% FPR	0.188, 8.298	0.206, 8.135
15% FPR	0.129, 5.197	0.117, 6.000
20% FPR	0.084, 4.649	0.083, 4.640

A comparison of Random Forest and logistic regression models using maternal demographics, estimated fetal weight, and Doppler parameters.

FPR, false positive rate.

Estimated fetal weight centile, Doppler parameters, and demographic parameters were used in the model.

Maternal demographic characteristics: Nulliparity, ethnicity, body mass index, smoking status, hypertensive disorders of pregnancy (HDP), BMI.

Doppler characteristics: **Doppler characteristics: Umbilical artery pulsatility index (PI) centile, middle cerebral artery PI centile, cerebroplacental ratio centile, uterine artery PI centile.

removing the EFW centile from the model, the CPR centile emerged as the most important sonographic feature.

CONCLUSION: Machine learning algorithms can predict the development of a growth-restricted neonate at term using routine data from a late third-trimester ultrasound scan with a high degree of accuracy, similar to that of traditional logistic regression models. The variables contributing most significantly to the machine learning models were the EFW centile, followed by the CPR and, to a lesser extent, other Doppler parameters. Future studies should aim to externally validate and practically implement these models in clinical settings to maximize their potential benefits.

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SUPPLEMENTARY TABLE 1

Baseline demographic, clinical, and sonographic characteristics of the study cohort according to whether they resulted in a growth-restricted neonate or not

Maternal and pregnancy characteristics	FGR (n = 182)	Controls (n = 14,735)	*P* value
Maternal age in y, median (IQR)	31.7 (27.2–36.6)	33.3 (29.8–36.3)	***<.001***
Nulliparity, n (%)	125 (68.7)	7485 (50.8)	***<.001***
Maternal ethnicity, n (%)			
White (1)	57 (31.3)	7196 (48.8)	***<.001***
Black (2)	20 (11.0)	1564 (10.6)	.870
Asian (3)	61 (33.5)	2465 (16.7)	***<.001***
Mixed (4)	10 (5.5)	570 (3.9)	.259
Other (5)	34 (18.7)	2940 (20.0)	.670
Fertility treatment, n (%)	10 (7.9)	743 (6.7)	.582
Previous stillbirth, n (%)	0 (0.0)	33 (0.5)	.590
Smoker, n (%)	19 (10.4)	447 (3.0)	***<.001***
Alcohol, n (%)	2 (1.1)	108 (0.7)	.567
Maternal BMI at booking in kg/m2, median (IQR)	24.0 (21.0–27.0)	24.4 (22.0–28.0)	***.012***
Gestational diabetes, n (%)	17 (9.3)	1756 (11.9)	.286
Hypertensive disorders of pregnancy, n (%)	15 (8.2)	453 (3.1)	***<.001***
Induction of labor, n (%)	107 (58.8)	5200 (35.3)	***<.001***
Gestational age at ultrasound in wk, median (IQR)	36.0 (36.0–36.0)	36.0 (36.0–36.0)	.451
Estimated fetal weight centile, median (IQR)	19.7 (8.8–33.0)	61.3 (44.4–76.7)	***<.001***
Abdominal circumference centile, median (IQR)	15.6 (6.3–30.4)	56.0 (38.7–72.4)	***<.001***
Gestational age at birth in wk, median (IQR)	39.0 (37.0–40.0)	39.0 (39.0–40.0)	***<.001***
Scan to birth interval in wk, median (IQR)	3.0 (1.0–4.0)	3.0 (3.0–4.0)	***<.001***
Birthweight in grams, median (IQR)	2350 (2160–2500)	3400 (3100–3700)	***<.001***
Birthweight centile, median (IQR)	2.1 (1.2–2.5)	59.5 (34.2–81.4)	***<.001***
Umbilical artery PI centile, median (IQR)	58.3 (36.1–80.9)	43.7 (21.1–65.7)	***<.001***
Middle cerebral artery PI centile, median (IQR)	39.6 (19.1–66.3)	53.3 (30.8–75.3)	***<.001***
Cerebroplacental ratio centile, median (IQR)	37.7 (20.0–67.4)	59.5 (38.4–79.1)	***<.001***
Uterine artery PI centile, median (IQR)	52.4 (20.2–90.0)	36.7 (16.3–66.8)	***<.001***

Italicized bold values indicate statistical significant.

BMI, body mass index; *FGR*, fetal growth restriction; *GA*, gestational age; *IQR*, interquartile range; *PI*, pulsatility index.

SUPPLEMENTARY TABLE 2

Prediction models for growth-restricted neonates using Random Forest machine learning and traditional logistic regression with different variable combinations

Variables	AUROC (95% CI)	Shrinkage (%)	Sensitivity (10% FPR)
Logistic regression			
Umbilical artery PI centile only	0.632 (0.620–0.644)	−0.005	27%
Middle cerebral artery PI centile only	0.616 (0.604–0.628)	−0.005	23%
Cerebroplacental ratio centile only	0.666 (0.654–0.678)	0.007	28%
Uterine artery PI centile only	0.592 (0.581–0.604)	−0.001	25%
Estimated fetal weight centile only	0.908 (0.903–0.914)	0.006	67%
Demographic characteristics[a] and Doppler parameters[b]	0.812 (0.803–0.821)	−0.001	68%
EFW centile and Doppler parameters[b]	0.925 (0.920–0.931)	0.002	73%
EFW with demographic characteristics[a] and Doppler parameters[b]	0.945 (0.941–0.950)	0.002	83%
Random Forest machine learning			
Umbilical artery PI centile only	0.841 (0.833–0.849)	0.011	54%
Middle cerebral artery PI centile only	0.770 (0.760–0.780)	0.020	42%
Cerebroplacental ratio centile only	0.771 (0.761–0.781)	0.031	40%
Uterine artery PI centile only	0.740 (0.730–0.750)	0.029	40%
Estimated fetal weight centile only	0.930 (0.925–0.935)	0.020	78%
Demographic characteristics[a] and Doppler parameters[b]	0.840 (0.832–0.848)	0.002	71%
EFW centile and Doppler parameters[b]	0.968 (0.966–0.972)	0.009	93%
EFW with demographic characteristics[a] and Doppler parameters[b]	0.940 (0.936–0.946)	0.005	81%

AUROC, area under the receiver operator curve; *CI*, confidence interval; *EFW*, estimated fetal weight; *FPR*, false positive rate; *PI*, pulsatility index.

[a] Demographic characteristics: Nulliparity, ethnicity, body mass index, smoking, hypertensive disorders of pregnancy; [b] Doppler characteristics: Umbilical artery PI centile, middle cerebral artery PI centile, cerebroplacental ratio centile, uterine artery PI centile.