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Systematic Review

## Effectiveness of Doppler Indices in Predicting Adverse Perinatal Outcomes in Early and Late-Onset FGR: Systematic Review

AlHussain Sagr Al Hazmi<sup>1</sup>, Rawabi Almarri<sup>2</sup>, Faisal Talal Alsharif<sup>1</sup>, Saeed Tariq Saloom<sup>1</sup>, Bushra Ali S AlGhamdi<sup>3</sup>, Afnan Mgbel<sup>4</sup>, Hajar Rida M Almoqbel<sup>5</sup>, Hussam Salem Alshammari<sup>6</sup>, Babiker Mhgoub Babiker Abdoon<sup>1</sup>, Doaa Walid Abdulfattah<sup>7</sup>, Aisha Ahmad N Qumiri<sup>8</sup>, Saad Khaleel Alonze<sup>9</sup>

1. Obstetrics and Gynecology Department, Maternity Hospital, First Health Cluster, King Saud Medical City, Riyadh, Saudi Arabia
2. Obstetrics and Gynecology Department, Security Forces Hospital, Riyadh, Saudi Arabia
3. Obstetrics and Gynecology Department, King Faisal Medical Complex, Taif, Saudi Arabia
4. Obstetrics and Gynecology Department, Armed Force Hospital, Khamis Mushait, Saudi Arabia
5. Obstetrics and Gynecology Department, Maternity and Children Hospital, Al-Ahsa, Saudi Arabia
6. Obstetrics and Gynecology Department, Qatif Central Hospital, Qatif, Saudi Arabia
7. Obstetrics and Gynecology Department, King Khalid University Hospital, Riyadh, Saudi Arabia
8. Obstetrics and Gynecology Department, King Abdulaziz Hospital, Jeddah, Saudi Arabia
9. Obstetrics and Gynecology Department, King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia

### Abstract

**Background:** Doppler velocimetry guides monitoring in fetal growth restriction (FGR), and the most informative index differ by early- vs late-onset disease. We aimed to evaluate Doppler indices to predict adverse perinatal outcomes in early- and late-onset FGR.

**Methods:** We searched online databases and screened full-text original studies linking Doppler measures with perinatal outcomes in FGR.

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Data were extracted on design, sample size, FGR, onset definitions, Doppler markers, outcome composites, and predictive performance, AUC, sensitivity, and specificity. Findings were analyzed qualitatively, because thresholds and outcomes varied. **Results:** we include nine observational studies. Common markers were UA-PI, MCA-PI, uterine artery PI, and ratios; some studies assessed composite measures. Late-onset cohorts found moderate to high discrimination for selected predictors, whereas larger cohorts showed modest performance for UCR and CPR thresholds. Abnormal UA Doppler was more sensitive than low CPR for predicting SGA, with similar specificity. Early abnormal UA Doppler identified higher stillbirth risk but had low sensitivity. **Conclusion:** Doppler indices aid risk grouping in FGR, but accuracy varies by onset phenotype, marker choice, and outcome definition; we need standardized thresholds and outcome sets in practice.

## Keywords

Fetal growth restriction; Doppler ultrasound; cerebroplacental ratio; umbilical artery; middle cerebral artery; ductus venosus; adverse perinatal outcome

## Introduction

Fetal growth restriction (FGR) is a major contributor to morbidity and mortality, with longer-term neurodevelopmental and cardiometabolic complications (1). Two phenotypes are commonly described and are separated by timing of diagnosis at 32 weeks gestation: early suspected FGR (<32 weeks) and late suspected FGR (>32 weeks) (2). Early suspected FGR is characterized by placental insufficiency with abnormal perfusion at the maternal and fetal interfaces, a very small fetus, and profound Doppler deterioration including advanced venous changes (2). Late suspected FGR is more frequent, the fetus may not be small, and cerebral blood flow redistribution could be the main Doppler signal of compromise (2).

Management is monitoring and timed delivery, attempting to balance risks of prematurity against progressive hypoxemia and acidemia because there is no effective therapy to reverse placental dysfunction (1). Doppler velocimetry is central to this monitoring. In early-onset disease, deterioration is preceded by rising UA impedance and progression to absent end-diastolic velocities,

as decompensation evolves (2). DV findings reflect late cardiovascular compromise and are associated with increased risk of fetal death and morbidity (2). In late disease, indices incorporating fetal redistribution such as the cerebroplacental ratio are widely used, but reported prognostic performance varies and thresholds differ in studies (3). This systematic review evaluates the effectiveness of Doppler indices in predicting adverse perinatal outcomes in early and late onset FGR, focusing on which vessels and ratios provide the most clinically useful prediction in each setting.

## Methods

This systematic review planned to evaluate how well fetal Doppler indices predict adverse perinatal outcomes in early and late onset fetal growth restriction (FGR). A structured search was performed in online databases and platforms that provide full-text access. Search terms combined controlled vocabulary and keywords related to fetal growth restriction, intrauterine growth restriction, early-onset and late-onset, Doppler, umbilical artery, middle cerebral artery, uterine artery, ductus venosus, and cerebroplacental ratio (CPR) or related ratios (UCR, UPCR, CPUR), along with outcome terms including stillbirth, acidemia, Apgar, NICU admission, neonatal morbidity, and composite

adverse perinatal outcome. Reference lists of eligible articles were also screened to identify additional studies missed by database searching.

Eligible studies were original human research prospective or retrospective cohorts, case control studies, or diagnostic-accuracy analyses that included pregnancies affected by FGR, SGA; reported at least one Doppler index as a predictor, and; provided perinatal outcomes or a defined adverse composite outcome that allowed assessment of prognostic or predictive performance. Studies limited to multiple gestations or without extractable Doppler-outcome data were excluded. No restrictions were applied to country of origin. Only studies with accessible full text were considered.

Two stage screening was applied: titles, abstracts were reviewed first, followed by full text assessment of relevant records. From each included study, data were extracted into a standardized form covering: study design, setting, sample size, FGR definition and gestational-age window, classification as early- or late-onset when available, Doppler indices assessed, outcome definitions, and performance metrics AUC, sensitivity, and specificity. When studies reported several Doppler markers, the principal predictor reported by the authors or the best-performing marker for the primary adverse outcome was recorded.

Risk of bias and applicability were planned to be assessed using a diagnostic, prognostic framework (QUADAS-2 domains adapted to prediction studies), focusing on participant selection, timing of Doppler relative to outcome, blinding, standardization of outcome assessment, and completeness of follow-up. Because included studies differed in FGR definitions, gestational-age windows, Doppler thresholds, and outcome composites, results were analyzed qualitatively rather than pooled quantitatively.

## Results

We include nine studies most were observational designs, including prospective cohorts and retrospective analyses, with sample sizes ranging from small single-center comparisons to large population-based cohorts. Several studies focused on late-onset FGR (after 32 weeks), while others enrolled growth-restricted pregnancies in broader gestational windows without a strict early, late split. Definitions of FGR were not uniform, some studies used estimated fetal weight or abdominal circumference below the 10th percentile, while others used Doppler abnormalities into the case definition. This variation affected baseline risk and how abnormal Doppler was interpreted in studies.

In the included studies the most frequently evaluated arterial measures were umbilical artery (UA) PI, middle cerebral artery (MCA) PI, and derived ratios, especially CPR and UCR. Some studies extended assessment to uterine artery indices or venous Doppler markers. Outcome definitions also differed, many used composite adverse perinatal outcomes that included emergency cesarean for fetal distress, low Apgar scores, neonatal acidemia, NICU admission, or major neonatal morbidity; one study reported stillbirth performance specifically in relation to early abnormal UA Doppler.

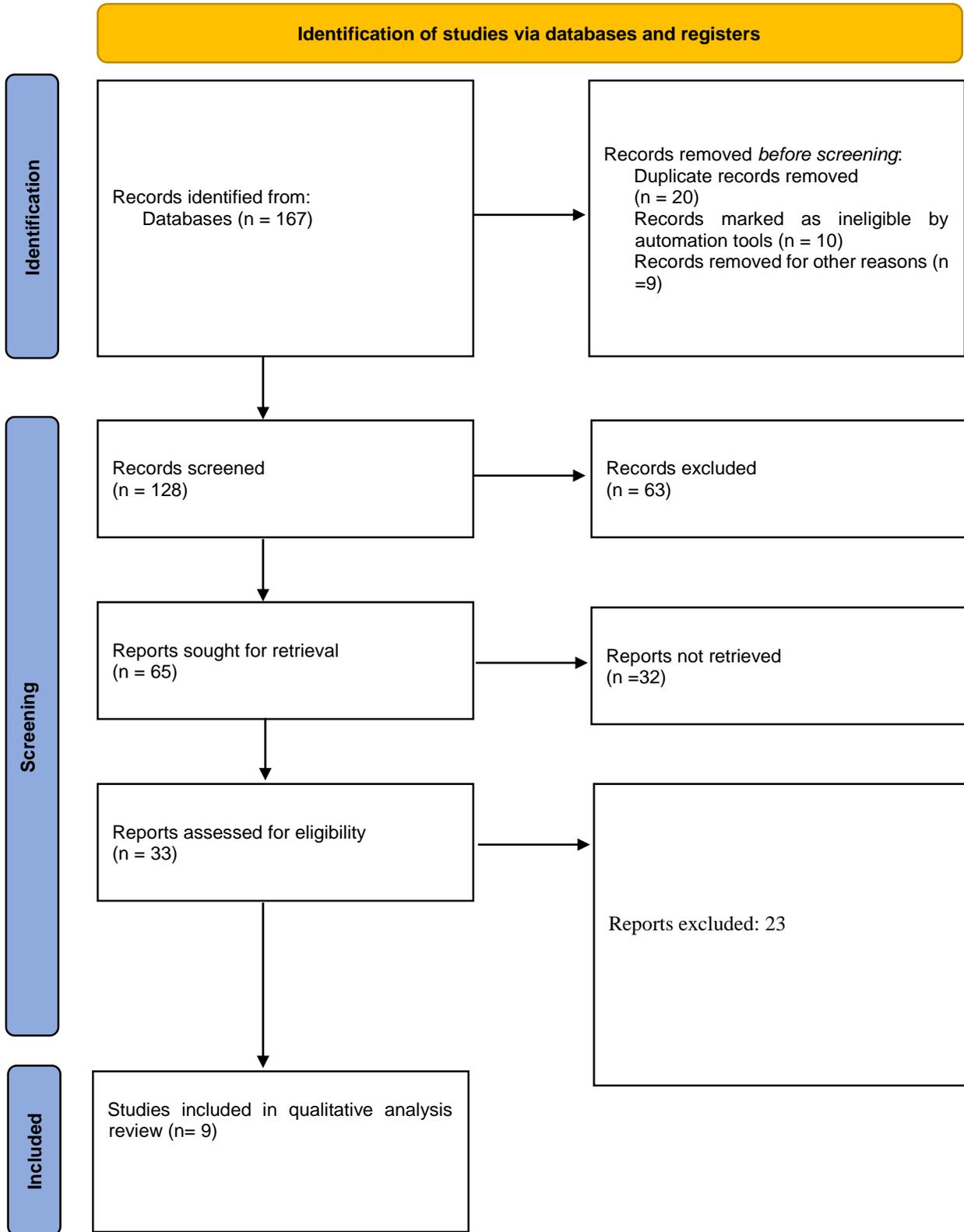
For late onset FGR, several studies reported moderate to high discrimination for selected Doppler derived predictors. Umbilical venous flow related measures showed strong performance in one late-onset cohort, with sensitivities in the high range and specificities the mid range for the chosen composite outcome. In another late onset dataset, specialized ratios (CPUR) and MCA-related measures (DDA) produced very high AUC estimates ( $>0.95$ ), though these findings came from smaller, comparison-style designs and not translate directly to broader populations. A large late-onset preterm

risk cohort reported more modest discrimination for UCR, CPR thresholds with balanced sensitivity and specificity around two-thirds.

One cohort found UA Doppler to have higher sensitivity than a low CPR threshold for identifying SGA and composite neonatal morbidity. For early gestational windows, abnormal UA Doppler before 30 weeks identified a higher-risk subgroup for stillbirth but with low sensitivity and high specificity.

UA, MCA, CPR-type indices consistently used clinically but direct comparison is limited by inconsistent FGR definitions, different gestational-age targets, and non-uniform outcome composites, leading to a narrative synthesis rather than a single pooled estimate. Characteristics of the included studies and main findings were presented in Table 1 and 2 respectively.

Fig 1: PRISMA flow chart



**Table 1. Included-study characteristics**

Study	Study Design	Sample Size	FGR Definition	Onset (Early, Late)	Doppler Indices Evaluated
Yang (2023) (4)	Prospective study	114	Late-onset FGR enrolled after confirmation	Late (Doppler performed 32+0 to 37+0)	UA-PI, MCA-PI, mean UtA-PI, CPR, UPCR
Dall'Asta et al (2020) (5)	Prospective cohort	468	Suspected FGR at 32+0–36+6 weeks; criteria included EFW, AC <10th or AC drop >50 centiles, etc.	Late (32+0–36+6)	Mean UtA-PI, UA-PI, MCA-PI, CPR
Wolf (2021) (6)	Cohort analysis of 856 singleton pregnancies “at risk for late-onset preterm FGR”	856	“At risk for late-onset preterm FGR”	Late-onset preterm	UCR, CPR
Leavitt 2022 (7)	Observational cohort	199 met inclusion with CPR	FGR defined as EFW <10th percentile (Hadlock)	Mixed GA	UA-PI, MCA-PI, CPR
Yilmaz (2023) (8)	Prospective cohort	141	Late-onset FGR, 32 to 39 weeks	Late (32–39 weeks)	UV blood flow (UVBF), UA-PI, MCA-PI, CPR, UtA-PI, DV-PI, UVBF, EFW, CPUR
Karabay (2025) (9)	Case–control style comparison	45 FGR + 45 control	Late FGR: diagnosis after 32 weeks; EFW <10th plus UA-PI >95th and, or CPR <5th	Late (>32 weeks)	DDA (MCA), CPR, UCR, CPUR
Adedo (2022) (10)	Comparative recruitment of FGR vs controls	180	Subjects: EFW <10th percentile	Mixed (28–40 weeks; not split early, late)	Umbilical artery Doppler indices
Lewkowicz (11)	NR (design details not)	NR	NR	Early-focused finding	Umbilical artery Doppler

Study	Study Design	Sample Size	FGR Definition	Onset (Early, Late)	Doppler Indices Evaluated
	captured in extracted lines)			(abnormal UA Doppler before 30 weeks)	
Hertting (2025) (12)	Retrospective cohort (implementation study)	5499	Exposure was whether CPR was used, reported; FGR, SGA definitions and Doppler thresholds NR in extracted lines	Mixed	CPR

**Table 2. Outcomes and predictive performance**

Study	Primary Adverse Outcomes	Key Doppler Predictor	Predictive Value (AUC, Sens, Spec)	Key Conclusion
Yang (2023) (4)	Composite adverse outcome: emergency CS for distress, UA pH <7.10, 5-min Apgar <7, neonatal special care admission (no stillbirth in cohort)	UPCR	AUC 0.824 (Sens, Spec NR in extracted lines)	UPCR independently associated with adverse outcomes; improves prognostic prediction in late-onset FGR
Dall'Asta et al (2020) (5)	Adverse perinatal outcome	EFW percentile at diagnosis (non-Doppler), and Dopplers added to models	EFW percentile AUC 0.847 (Sens 82%, Spec 81%)	At diagnosis of late-onset FGR, EFW percentile showed strong discrimination; Doppler indices contributed less alone

Study	Primary Adverse Outcomes	Key Doppler Predictor	Predictive Value (AUC, Sens, Spec)	Key Conclusion
Wolf (2021) (6)	Composite adverse perinatal outcome	UCR $\geq 0.9$ or CPR $< 1.11$	Model AUC 0.73; Sens 70%, Spec 64%	UCR, CPR thresholds were associated with composite adverse outcome; performance depends on reference charts but overall moderate discrimination
Leavitt 2022 (7)	Primary: neonatal SGA $< 10^{\text{th}}$ ; Secondary: pH $< 7.10$ , Apgar $< 7$ , NICU, RDS, hypoglycemia; composite of secondary outcomes	Abnormal UA Doppler vs low CPR ( $< 1.081$ )	UA Doppler sensitivity for SGA 12.8% vs CPR 4.4%; specificity similar (95–96%)	UA Doppler had higher sensitivity than CPR for predicting SGA and composite adverse neonatal outcome in this cohort
Yilmaz (2023) (8)	Adverse perinatal outcome	UVBF	UVBF AUC 0.848, Sens 87%, Spec 65%; CPUR AUC 0.820; DV-PI AUC 0.822; others reported	In late-onset FGR, umbilical venous flow–related measures showed higher predictive performance for adverse outcome than some arterial indices
Karabay (2025) (9)	Adverse perinatal outcome	DDA (MCA) and CPUR	DDA AUC 0.966; CPUR AUC 0.959	DDA and CPUR showed very high discrimination for adverse outcomes in late FGR vs controls in this dataset
Adedo (2022) (10)	Adverse perinatal incidents higher in FGR	UA Doppler indices (PI, RI, S-D; abnormal waveform)	AUC, Sens, Spec NR in extracted lines	FGR fetuses had higher UA Doppler indices and more abnormal waveforms, with more adverse perinatal incidents than controls

Study	Primary Adverse Outcomes	Key Doppler Predictor	Predictive Value (AUC, Sens, Spec)	Key Conclusion
Lewkowitz (11)	Stillbirth risk highlighted	Abnormal UA Doppler before 30 weeks	Stillbirth in abnormal- UA group 13.8%; Sens 21.1%, Spec 93.4%, AUC 0.58	Abnormal UA Doppler before 30 weeks identified a subgroup with higher stillbirth risk, but with low sensitivity
Hertting (2025) (12)	Perinatal morbidity, mortality composite reported; study focus was identification, management changes	CPR reporting, implementation	AUC, Sens, Spec NR	Study evaluated clinical impact of implementing CPR reporting in ultrasound practice rather than classic diagnostic-accuracy metrics

## Discussion

Our study addressed which Doppler indices separate fetuses likely to deteriorate from those who can be monitored safely, and does the answer differ between early and late disease. The framework is supported by the recognized phenotypic split. Early suspected FGR is a placental-insufficiency dominant state, with abnormal uterine and umbilical perfusion and a higher probability of progressive Doppler deterioration. Late suspected FGR is more diagnostically challenging because placental perfusion measures remain normal, while cerebral redistribution is the only Doppler sign (2). These differences help explain why studies assessing UA, MCA, CPR, and venous Doppler do not get uniform predictive estimates in gestations and populations.

A consistent theme in the literature is heterogeneity, both in what constitutes and in how is defined. In a large prognostic accuracy synthesis comparing CPR and MCA Doppler with UA Doppler, sensitivities and specificities and thresholds varied, and prediction intervals were large, reflecting substantial between-study variability (3). This matters clinically: shifting a CPR cutoff changes the balance between missed cases and false alarms, which in turn affects intervention rates. Even when pooled comparisons suggest CPR outperform UA for certain composite outcomes or emergency delivery for fetal distress, uncertainty remains about the subgroups in which this holds (3).

A one-stage individual participant data meta-analysis found that CPR alone and UA PI alone had very similar discrimination for adverse perinatal outcome, and adding CPR to UA PI increased the AUC only minimally (3). This does not mean CPR is useless, it suggests that, in mixed-risk singleton populations, CPR not add much beyond UA PI for broad composites. That conclusion sits alongside other reviews that report moderate diagnostic

performance for CPR in specific outcomes but more limited performance for operative delivery or NICU admission (13). The literature supports a cautious interpretation, CPR can capture redistribution physiology, but its predictive value is not guaranteed and depends on phenotype, outcome, and how thresholds are applied.

For early-onset FGR, venous Doppler is positioned as a marker of late decompensation. Absent and reversed DV a-wave reflects increased end-diastolic intracardiac pressure and worsening cardiovascular compromise, and is linked to higher mortality and morbidity risk (2). In clinical datasets, pathological DV patterns have been associated with severe adverse neonatal status, including acidosis and composite morbidity (14). The practical implication is that DV less about early warning and more about identifying the point where continued expectant management becomes unsafe, mainly relevant when prematurity risk drives reluctance to deliver.

Broader peripartum Doppler data in term populations shows that abnormal UA Doppler, CPR, and UV pulsations are associated with fetal distress and operative delivery for suspected distress (15). The studies supports Doppler as essential to FGR risk stratification, but also highlights why a single best index is unlikely in all gestations. Standardization of FGR definitions, Doppler thresholds, and outcome sets is critical for producing estimates that translate into consistent clinical decision rules (3).

## Conclusion

Doppler velocimetry is central to surveillance in FGR, but no single index performs best in all settings. Evidence from included studies indicate that late-onset FGR may be is larger datasets show only modest discrimination for common CPR and UCR thresholds. In early-onset disease, worsening

placental resistance and venous Doppler abnormalities reflect escalating cardiovascular compromise and higher risk.

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