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Role of First- and Second-Trimester Uterine Artery Doppler in Predicting Adverse Pregnancy Outcomes: A Review of Literature

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Abstract

Background: *Uterine artery Doppler velocimetry (UADV) is a non-invasive tool for assessing uteroplacental blood flow and identifying pregnancies at risk for pre-eclampsia (PE), fetal growth restriction (FGR), and small for gestational age (SGA). While abnormal indices such as elevated pulsatility index (PI), resistance index (RI), and persistent bilateral notching have been consistently associated with placental insufficiency, the clinical value of UADV depends on the timing of assessment, threshold definitions, and integration with other screening modalities.*

Methods: *This review synthesises evidence from eight high-quality studies published between 1998 and 2023, encompassing large multicentre prospective cohorts, randomised controlled trials, and meta-analyses. The studies varied in gestational age at Doppler assessment (first trimester, mid-trimester, and serial approaches), measurement technique (transabdominal or transvaginal), and criteria for abnormality (centile-based thresholds or fixed cut-offs). Outcomes assessed included PE, FGR, SGA, and composite maternal-fetal morbidity.*

Results: *Mid-trimester UADV demonstrated the strongest standalone predictive value, with detection rates of up to 69–93% for severe early-onset PE and FGR and ~60% for early PE/IUGR in a large randomised trial [1,2]. First-trimester Doppler alone had modest sensitivity for overall PE and SGA but was more predictive of severe phenotypes, with Martin et al. (2001) reporting 60% detection for PE requiring delivery before 32 weeks. Incorporation into multimodal algorithms, as in the ASPRE trial, achieved 76.7% detection of preterm PE at a 10% false-positive rate and, when combined with aspirin prophylaxis, reduced preterm PE incidence by over 60% [3]. Smaller cohort studies and a large meta-analysis reinforced the predictive role of UADV across gestation, with the highest effect sizes in mid-to-late pregnancy.*

Conclusion: *The evidence consistently supports UADV as a valuable screening tool, particularly for early-onset, severe placental disease. Mid-trimester measurement offers the best standalone perfor-*

mance, while first-trimester assessment gains maximum utility within integrated risk models that link detection to effective interventions. Limitations include heterogeneity in technique, population differences, and the limited impact of Doppler-only strategies on outcomes without accompanying treatment pathways. This synthesis underpins the rationale for including UADV in structured screening programmes and informs the methodological approach of the present thesis.

Keywords: Uterine artery Doppler, pre-eclampsia, fetal growth restriction, small for gestational age, screening, prediction, pregnancy outcomes.

Introduction

Hypertensive disorders of pregnancy, fetal growth restriction (FGR), and small-for-gestational-age (SGA) infants collectively account for a significant proportion of global maternal and perinatal morbidity and mortality [4,5]. Preeclampsia (PE), a hallmark hypertensive disorder, affects 2–8% of pregnancies globally and remains one of the leading causes of medically indicated preterm births and maternal deaths, particularly in low- and middle-income countries (LMICs), where access to consistent antenatal care is often inadequate [4].

FGR and SGA, while clinically distinct entities, share a common etiological basis rooted in defective placentation and impaired uteroplacental perfusion [4,5]. Normally, during early pregnancy, extravillous trophoblasts invade the spiral arteries of the uterus, converting them from narrow, high-resistance vessels into dilated, low-resistance conduits that facilitate adequate placental and fetal perfusion [4]. This vascular remodelling proceeds in two stages: the first involves invasion into the decidua before 12 weeks, and the second involves deeper penetration into the myometrium between 12 and 16 weeks of gestation [4,5]. Failure of this physiological transformation underlies many of the complications associated with PE, FGR, and SGA [5,6].

Uterine artery Doppler velocimetry (UADV) has emerged as a valuable, non-invasive modality to assess the adequacy of uteroplacental circulation [4,7]. By analysing blood flow waveforms in the uterine arteries and quantifying indices such as the pulsatility index (PI), resistance index (RI), systol-diastolic (S/D) ratio, and the presence of early diastolic notching, UADV allows for early identification of pregnancies at risk of adverse outcomes [5,6]. These Doppler parameters serve as surrogates for vascular impedance; elevated PI or RI and the persistence of bilateral notching suggest increased resistance in the uterine arteries, indicative of incomplete spiral artery remodelling (5;8).

The utility of UADV lies in its ability to predict pregnancy complications even before clinical symptoms manifest 4. Studies have shown that abnormal uterine artery Doppler indices precede the onset of PE and FGR by several weeks, offering a critical window for timely surveillance and prophylactic interventions such as low-dose aspirin administration (4,6).

Importantly, the predictive accuracy of UADV is highly dependent on the gestational age at which it is performed (4,7). First-trimester UADV, typically between 11 and 14 weeks, offers an early opportunity to identify high-risk pregnancies (4).They demonstrated that uterine artery Doppler indices obtained during the first trimester could predict a

spectrum of pregnancy complications, although sensitivity remained moderate when used in isolation (4). A meta-analysis by Velauthar et al., involving over 55,000 women, confirmed that elevated PI and bilateral notching during the first trimester were significantly associated with adverse outcomes, but also emphasized the limitations of UADV alone (5).

To enhance predictive performance, several studies have explored combining UADV with maternal serum biomarkers and clinical risk factors (6).They proposed a model that incorporated uterine artery PI with maternal characteristics and demonstrated improved predictive capacity for PE and SGA when compared to Doppler use alone (6). These findings support the concept that a multiparametric approach, rather than reliance on a single modality, yields more accurate risk stratification (5,6).

In contrast to first-trimester assessments, second-trimester UADV—especially between 22 and 24 weeks—has shown greater diagnostic accuracy in predicting early-onset PE and FGR (7).This study reported that uterine artery PI > 95th percentile measured at 23–24 weeks was associated with a significantly higher risk of adverse pregnancy outcomes in high-risk populations (7). The study advocated for second-trimester UADV as an effective triage tool to select candidates for intensified antenatal surveillance (7). Similarly, Acharya et al. established reference ranges for Doppler indices during the second half of pregnancy, facilitating the identification of deviations from normal uterine artery resistance trends (9).

The natural decline in uterine artery impedance typically observed during pregnancy is due to continued placental vascular remodelling (9). If resistance remains elevated beyond the second trimester, it often signals underlying placental insufficiency (8). This study found that pregnancies complicated by PE often showed persistent Doppler abnormalities and that similar findings in subsequent pregnancies were linked to a higher recurrence risk (8). This reinforces the importance of Doppler as both a diagnostic and prognostic tool, particularly for women with a prior history of hypertensive disorders (8).

Beyond prediction of PE and FGR, UADV has also been evaluated in the context of recurrent pregnancy loss (RPL) (10).They investigated the role of the uterine radial artery resistance index and found it to be predictive of reproductive outcomes in women with RPL and thrombophilia (10). This highlights the expanding utility of Doppler assessment in broader reproductive medicine contexts, beyond conventional obstetrics (11).

Despite the growing body of supportive evidence, the translation of UADV into routine obstetric practice faces several challenges (4). One major barrier is the lack of standardized normative values across diverse populations (9). Many Doppler reference ranges are derived from Caucasian cohorts, which may not be applicable in LMIC settings such as India or Sub-Saharan Africa, where baseline vascular physiology and maternal health profiles differ significantly (9,11). Additionally, variability in operator skill and equipment quality can affect measurement reliability, necessitating structured training and quality control systems (4).

Nevertheless, the scalability and affordability of Doppler technology make it a highly attractive tool for resource-constrained settings (4). Portable de-

vices, coupled with recent advancements in telemedicine and artificial intelligence–assisted waveform interpretation, offer promising solutions for extending UADV access to peripheral centres (4). With appropriate contextual adaptation and integration into national antenatal care protocols, UADV could serve as a cornerstone of prenatal risk screening in LMICs (4).

UADV provides a physiologically grounded, evidence-based, and cost-effective means of identifying pregnancies at heightened risk for PE, FGR, and SGA (4;5). While its predictive performance varies with gestational age and population characteristics, its utility is most pronounced when integrated into multi-modal screening frameworks (5). The next frontier in Doppler-based surveillance lies in the regional validation of indices and broader policy integration, particularly in settings where maternal and fetal health burdens remain high (9). Given the global push toward personalised, preventive obstetrics, UADV has the potential to bridge gaps in care and improve outcomes for mothers and babies alike (4).

Fig 1 depicts the normal uterine artery doppler velocimetry in non pregnant patient as well as in first , second and third trimester UADV in pregnant patients .Fig 2 depicts uterine artery notching which suggest increase in uterine artery resistance which is an indication of spiral artery dysfunction.

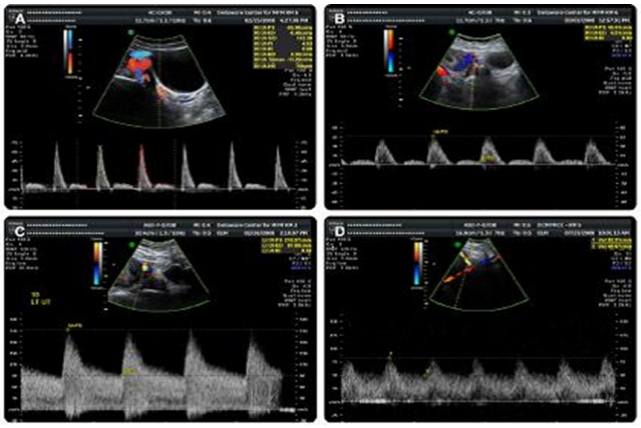

Fig. 1. Depiction of Uterine artery Doppler ultrasound in the nonpregnant and pregnant patient

A. Nonpregnant patient. B. 1st trimester. C. 2 nd trimester. D. 3rd trimester (Mariana et al , 2020) [12]

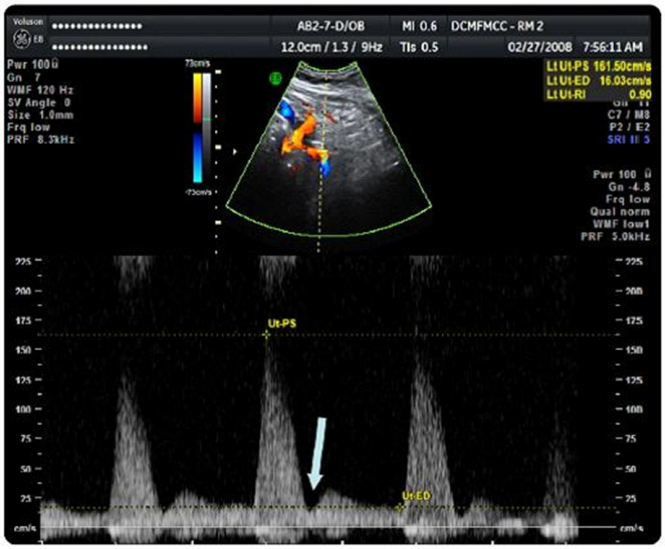

Fig 2 Uterine artery notching in doppler (Mariana et al , 2020) [12]

The primary aim of this systematic review is to evaluate the clinical utility and predictive performance of uterine artery Doppler velocimetry (UADV) in identifying pregnancies at risk for preeclampsia, fetal growth restriction (FGR), and small-for-gestational-age (SGA) outcomes.

Research questions :

1. What is the diagnostic accuracy of uterine artery Doppler velocimetry (pulsatility index, resistance index, and diastolic notching) in predicting preeclampsia, fetal growth restriction, and small-for-gestational-age outcomes?
2. How does the gestational age at the time of Doppler assessment influence its predictive effectiveness for adverse pregnancy outcomes?
3. Does integrating uterine artery Doppler indices with maternal risk factors improve the overall performance of screening models for

preeclampsia, fetal growth restriction, and small-for-gestational-age infants?

Methods

Search Strategy

A structured literature search was conducted to identify studies evaluating the role of uterine artery Doppler velocimetry (UADV) in predicting preeclampsia (PE), fetal growth restriction (FGR), and small-for-gestational-age (SGA) outcomes. The search was performed in PubMed, Scopus, EMBASE , and COCHRANE for publications from January 1, 1998, to July 31, 2025. Search terms combined free text and MeSH keywords as follows: ("Uterine artery Doppler" OR "uterine artery velocimetry") AND ("Pulsatility Index" OR "Resistance Index" OR "Notching") AND ("Preeclampsia" OR "Fetal Growth Restriction" OR "Small for Gestational Age"). Filters were applied to restrict results to human studies, English language, and clinical research designs, including randomised controlled trials, cohort studies, cross-sectional studies, and meta-analyses. The reference lists of eligible studies were manually screened to identify additional relevant publications. Grey literature, preprints, and non–peer-reviewed sources were excluded.

Information Sources

Four electronic databases, PubMed , Scopus , EMBASE AND COHRANE were selected for their comprehensive coverage of peer-reviewed literature in obstetrics, maternal-fetal medicine, and diagnostic imaging. Both were searched systematically using the same search terms and filters. Reference lists of all shortlisted articles were also reviewed to capture studies not identified through the database searches. Only peer-reviewed, full-text publications in English were included, and no grey literature or unpublished sources were considered.

Study Selection

Independently Reviewed and screened all retrieved citations. Titles and abstracts were first assessed for relevance, followed by full-text review to determine eligibility. Studies were included if they met the following criteria: original research (prospective cohort, cross-sectional, RCT, or meta-analysis); population of pregnant women undergoing UADV between 11 and 24 weeks' gestation; intervention involving transvaginal or transabdominal assessment of pulsatility index (PI), resistance index (RI), and/or bilateral notching; outcomes including PE, FGR, or SGA with correlation to Doppler parameters; published in English; and indexed in PubMed or Scopus.

Studies were excluded if they were editorials, opinion pieces, case reports, conference abstracts, animal studies, or basic science reports without clinical correlation; if they lacked outcome data or Doppler indices; if they were in languages other than English; or if they did not report gestational timing of Doppler assessment. Disagreements on study inclusion were resolved by discussion or, if necessary, consultation with a third reviewer. Ultimately, eight high-quality studies meeting all criteria were included, comprising a mix of prospective cohorts, RCTs, cross-sectional designs, and one meta-analysis.

Data Collection

Data collection was standardized using a predesigned Microsoft Excel form, which was piloted on two studies to ensure clarity and completeness. This form recorded study identifiers, participant characteristics, Doppler measurement parameters, and outcome definitions. It was designed to ensure consistent recording of information across all included studies.

Data Extraction

Data extraction was performed independently by two reviewers, capturing details such as authors, year, country, study design, sample size, gestational age at Doppler, population risk category, Doppler indices (PI, RI, notching), imaging mode, clinical outcomes (PE, FGR, SGA), and diagnostic performance metrics (sensitivity, specificity, predictive values, odds ratios, and AUC). All extracted data were cross-checked for accuracy, and any discrepancies were resolved by consensus after reviewing the source articles.

Results

Literature Search

This systematic review followed PRISMA 2020 guidelines for literature identification, screening, and inclusion. An initial pool of 128 articles was retrieved from PubMed, Scopus, Emboss and Cochrane filtered for human studies published in English between 1998 and 2023 in English. Following removal of duplicates (n=16), 112 unique records were screened based on titles and abstracts. A total of 86 full-text articles underwent eligibility assessment. Of these, 78 were excluded due to the following: lack of Doppler data (n=17), non-reporting of PE/FGR/SGA outcomes (n=23), gestational windows outside 11–24 weeks (n=19), non-original design such as editorial/commentary (n=7) / absence of validated indices like PI, RI / bilateral notching (n=12) (Table 1, Fig 3).

Figure 3: PRISMA 2020 Flow Diagram for Study Selection Process

	Number of Articles	Rationale
Lack of Doppler data		Articles did not perform or report uterine artery Doppler assessments despite discussing hypertensive disorders or FGR.
Non-reporting of PE, FGR, or SGA outcomes	23	Studies applied Doppler but did not link findings to the primary obstetric outcomes of interest.
Gestational windows outside 11–24 weeks	19	UADV assessments performed outside the first and second trimester (either too early or late), which could skew predictive validity.
Editorials, reviews, or commentaries (non-original work)	7	Non-primary literature was excluded as per protocol (no original data for extraction).
No validated Doppler indices reported (PI, RI, notching)	12	Doppler used, but without reporting standardized indices, cut-offs, or statistical associations.

Table 1: Exclusion Criteria Applied to Full Texts

Characteristics of Studies

The final selection included 8 high-quality studies that met all inclusion criteria. These comprised 2 randomised controlled trials (RCTs), 5 prospective cohort studies, and 1 systematic review and meta-analysis. All studies were peer-reviewed, indexed in major databases, and used standardised Doppler methodologies (Table 2).

Ref No.	Author (Year)	Title	Place	Country	Study Design	Level of Evidence	Sample Size	GA at UADV	Criteria	Outcomes	Key Strengths	Key Limitations	Certainty Rating
1	Kurdi et al. (1998)	The role of colour Doppler imaging of the uterine arteries at 20 weeks in the prediction of adverse pregnancy outcome	Birmingham	UK	Prospective cohort	II	1,022 (946 analysed)	20 weeks	Bilateral notches ± mean RI > 0.55	PPV ≈ 46% for major outcomes with composite	Simple, reproducible cut-offs; anomaly-scan embedment	Modest N; inter-observer notch variability; no multivariable adjustment	Moderate
2	Papageorghiou et al. (2001)	Uterine artery Doppler at 23 weeks in the prediction of pre-eclampsia and intrauterine growth restriction	Multicentre, 7 hospitals	UK	Prospective cohort	II	8,202 (7,851 outcomes)	23 weeks	PI > 95th centile; bilateral notching	Sensitivity: 69% (PE+FGR), 24% (PE without FGR), 13% (FGR); early-delivery detection up to 93%	Large pragmatic cohort; centile-based cut-offs; high technical success rate	No biomarkers; single time-point; limited diversity	High
3	Martin et al. (2001)	Screening for pre-eclampsia and fetal growth restriction by uterine artery Doppler at 11–14 weeks	London, multicentre	UK	Prospective cohort	II	3,324 (3,045 outcomes)	11–14 weeks	Mean PI > 2.35 (95th centile)	Sensitivity: 27% (all PE), 60% (<32 wk PE), 11.7% (FGR)	Early gestation window; clear thresholds	Modest sensitivity; no biomarkers; limited diversity	Moderate
4	Melchiorre et al. (2009)	First-trimester uterine artery Doppler indices in the prediction of adverse outcome	London	UK	Prospective cohort	II	3,010	11–14 weeks	RI > 90th and > 95th centiles; bilateral notching	AUC: 0.60 (SGA), 0.78 (preterm IUGR)	Large, blinded, prespecified methods	Limited for general SGA; SGA definition issues	High
5	Scandiuzzi et al. (2016)	Uterine artery Doppler in low-risk pregnancies: first and second trimester assessment	Minas Gerais	Brazil	Prospective cohort	II	162	11–14 weeks and 20–24 weeks	Mean RI/PI > 95th centile; combined with maternal factors	First-trimester RI > 95th OR ≈ 23 for HDP; model AUC 0.81	Integration of Doppler with maternal factors; protocolised single operator	Small sample; low event counts; low-risk cohort only	Moderate
6	García et al. (2016)	Do knowledge of uterine artery resistance in the second trimester and targeted surveillance improve pregnancy outcomes? (UTOPIA trial)	Spain	Spain	Randomised controlled trial	I	11,667	19–22 weeks	PI > 90th centile; targeted follow-up	Detection: ~59–60% early-onset PE/IUGR (FPR ~11%); no improvement in primary composite outcomes	Large RCT; pragmatic screening in anomaly scan	No effective treatment pathway; increased interventions without improved outcomes	High
7	Rolnik et al. (2017)	ASPRE trial: performance of screening for preterm pre-eclampsia in first trimester	Multicentre	Multiple countries	Prospective cohort within RCT screening programme	I	25,797	11–13 weeks	Combined model (maternal factors, MAP, UtA-PI, PAPP-A, PlGF)	Detection: 76.7% preterm PE, 43.1% term PE, ~10% screen-positive rate	Large international dataset; linked to prevention trial; robust methodology	Needs biomarker access; requires calibration to local populations	High
8	Zhi et al. (2023)	Association between uterine artery Doppler and small-for-gestational-age infants: a systematic review and meta-analysis	Multinational	Various	Systematic review/meta-analysis	I	41 studies	Any trimester	Abnormal PI/RI or notching	OR ≈ 3 (mid-pregnancy PI >95th) and OR ≈ 6 (late pregnancy PI >95th) for SGA; pooled PI + 0.21, RI + 0.05	Large pooled evidence; covers all trimesters	Heterogeneity in thresholds/equipment; study-level data	High

Table 2: Characteristics of Included Studies

Risk of Bias Assessment

The overall methodological quality of the included studies was moderate-to-high, though specific limitations warrant caution in interpretation. Large multicentre cohorts such as Papageorghiou et al. (2001) and Rolnik et al. (2017) demonstrated low selection bias through prospective recruitment, standardised Doppler protocols, and high follow-up completeness (>95%)(1,3). However, several earlier single-centre studies (13,15) had modest sample sizes and outcome counts, raising the potential for imprecision and type II error. Detection and performance metrics were generally derived from prespecified thresholds,

limiting analytical flexibility bias; nonetheless, variation in cut-offs (e.g., 90th vs 95th centile) and outcome definitions introduces heterogeneity. Blinding of outcome assessors to Doppler results was explicitly reported in only half of the studies, introducing a possible measurement bias. Randomised designs such as García et al. (2016) and the interventional ASPRE trial reduced confounding, yet their generalisability may be constrained by specific healthcare settings and baseline risk profiles(2,3). The meta-analysis by Zhi et al. (2023) provided pooled effect estimates but was limited by study-level data and substantial heterogeneity in Doppler acquisition techniques(17). Across studies, the risk of selective reporting was low, with outcomes clearly defined and statistical analyses aligned with study objectives. Nevertheless, absence of individual participant data meta-analysis and inconsistent adjustment for maternal risk factors limit the precision of pooled estimates and may inflate observed associations in unadjusted analyses.

Results of the Studies

Across the eight included studies, there was considerable variation in study design, gestational age at UADV, Doppler criteria used, and outcome definitions, but all consistently demonstrated that abnormal uterine artery Doppler findings — particularly elevated pulsatility index (PI), resistance index (RI), and bilateral notching — were associated with increased risks of pre-eclampsia (PE), fetal growth restriction (FGR), small-for-gestational-age (SGA) neonates, and related adverse perinatal outcomes.

Kurdi et al. (1998) explored a “one-stop” screening strategy by incorporating colour Doppler UADV into the routine 20-week anomaly scan in 1,022 pregnancies, of which 946 were analysable after exclusions. Abnormal results were defined by the presence of bilateral notching and/or a mean RI > 0.55. Bilateral notching was particularly predictive of PE, with the highest positive predictive value (~46%) achieved when both bilateral notching and elevated RI were present (13) This simple combination identified pregnancies at significantly increased risk for PE, SGA <5th centile, and perinatal death.

The study was significant in suggesting that Doppler could potentially be used to guide differentiated antenatal surveillance, laying the groundwork for risk-based obstetric care. Strengths included its integration into an existing universal visit and use of straightforward, reproducible Doppler thresholds. However, the study was limited by modest numbers of adverse outcomes (21 PE cases; 57 SGA cases) and the absence of adjustment for potential confounders. Additionally, notch assessment introduces potential inter-operator variability, which the study did not formally quantify. Although Kurdi et al. (1998) were pivotal in demonstrating the possible role of mid-trimester uterine artery Doppler in stratifying antenatal care, its age limits its contemporary relevance(13). 10Conducted with older imaging technology, without integration of maternal or biochemical markers, and focusing on 20-week assessment—well beyond the window for preventive interventions—its findings are now primarily of historical importance rather than clinical applicability.”

In one of the largest prospective cohorts to date, Papageorghiou et al. (2001) incorporated transvaginal UADV into the routine 23-week anomaly scan across seven UK maternity units, providing real-world performance data at a gestation coinciding with the completion of spiral artery remodelling.

Of 8,335 eligible singleton pregnancies, usable bilateral waveforms were obtained in 8,202 women (technical success rate 98.4%), and complete pregnancy outcomes were available for 7,851 (95.7%) (1). The median mean uterine artery PI was 1.04, with the 95th centile threshold set at 1.63. Bilateral notching was present in 9.3% of women and unilateral notching in 11.1%. Using PI > 95th centile, detection rates were 69% for PE with concomitant FGR, 24% for PE without FGR, and 13% for isolated FGR. Sensitivities improved substantially for early-onset disease requiring delivery before 32 weeks — in these severe subgroups, detection rates reached 93% for PE with FGR. Bilateral notching achieved similar sensitivities to PI > 95th but at the cost of higher screen-positive rates, underlining a classic trade-off between yield and false-positive burden.

This large-scale, pragmatic trial demonstrated excellent feasibility and provided clear centile-based thresholds, but its single time-point design and absence of biomarker integration limit direct comparability with modern multimarker risk algorithms.Another limitation of this study is that the moderate predictive performance reported with limited sensitivity, particularly for late-onset PE and small-for-gestational-age infants, and a relatively high false-positive rate. The study's restriction to a single gestational age (23 weeks) and the use of transvaginal Doppler limit its generalizability and routine clinical applicability.

Martin et al. (2001) targeted an earlier screening window, performing transabdominal UADV at 11–14 weeks in 3,324 pregnancies across three London hospitals. Complete follow-up was available for 3,045 cases. The 95th centile for mean PI was 2.35, with little variation across the narrow gestational range(14). As a standalone screen, PI > 2.35 detected 27% of PE cases overall, with markedly better performance for early-onset PE requiring delivery before 32 weeks (60% sensitivity, specificity 88%). Detection of FGR was lower at 11.7%, with the most benefit again in more severe phenotypes. These results confirmed the biological plausibility of impaired placentation being detectable in the first trimester but also emphasised that Doppler alone — at an acceptable false-positive rate — lacks the sensitivity needed for universal early screening. The authors noted that integration with clinical and biochemical markers would likely improve early predictive performance, a finding subsequently borne out by later combined-model studies.

The study was also methodologically sound, with a systematic assessment of uterine artery pulsatility index and clear outcome definitions. However, several limitations reduce its clinical applicability. The sample size was relatively small compared to later multicenter studies, limiting the statistical power and precision of predictive values.

Melchiorre et al. (2009) investigated the predictive role of first-trimester UADV in 3,010 singleton pregnancies at 11–14 weeks, specifically for SGA and intrauterine growth restriction (IUGR) (15). The 90th and 95th centiles for RI were 0.82 and 0.85, respectively. Overall, 9.0% of the cohort had RI values above the 90th centile and 4.5% above the 95th. Bilateral notching was present in ~45% of cases, with a higher prevalence among those delivering SGA infants (56% vs 43%). Median RI was also significantly higher in the SGA group (0.74 vs 0.70). Receiver operating characteristic analysis yielded an AUC of 0.60 for SGA overall, improving to 0.78 for preterm IUGR, indicating greater

discriminatory ability for severe, early placental disease. The authors noted that defining SGA solely by birthweight may obscure pathophysiological subgroups and dilute predictive accuracy — a caution particularly relevant for screening studies in mixed-risk populations.

The strength of this study lies in its prospective design and the separate analysis of SGA and IUGR, recognizing that not all small fetuses are growth-restricted. However, predictive accuracy is modest, with relatively high false-positive rates, limiting the test's clinical utility as a stand-alone screening tool. The reliance on birthweight centiles (<10th) to define SGA also introduces heterogeneity, since constitutionally small but healthy infants may have been misclassified.

Scandiuzzi et al. (2016) conducted a prospective cohort study in 162 low-risk Brazilian women, performing UADV in both the first (11–14 weeks) and second (20–24 weeks) trimesters(16). Elevated mean RI (>95th centile) in the first trimester — even if normalised later — remained a strong independent predictor of hypertensive disorders of pregnancy (adjusted odds ratio ≈ 23). When combined with maternal demographic and obstetric history, first-trimester mean RI improved the model's predictive performance (AUC 0.81). The use of a single experienced operator and protocolised methodology strengthened internal validity, though the small sample and low event rates limit generalisability. This study importantly highlighted that some women with early abnormal uteroplacental impedance remain at risk even if Doppler indices appear normal later in gestation.

The strengths of this study include its prospective design, focus on a low-risk population, and comparison of first-versus second-trimester Doppler performance, which directly addresses the timing of optimal screening. This comparative approach adds nuance to the literature, as much earlier work concentrated on high-risk cohorts. However, several limitations constrain its clinical applicability. Predictive accuracy was modest, with relatively low sensitivity and specificity, suggesting that uterine artery Doppler alone is insufficient for population-wide screening.The reliance on perinatal outcomes such as "adverse neonatal events" without precise subclassification also weakens interpretability, as outcomes of differing pathophysiological origin may have been pooled.

García et al. (2016) reported the UTOPIA trial, a large RCT of 11,667 unselected women randomised at the 19–22-week anomaly scan to standard care versus disclosure of UtA-PI results (>90th centile) and enhanced surveillance(2) Abnormal screening identified ~59–60% of early-onset PE/IUGR cases at an 11% false-positive rate. However, disclosure and targeted follow-up did not improve the composite of adverse maternal and perinatal outcomes compared with routine care, despite more interventions (including antenatal corticosteroids and earlier delivery). These findings underline that effective outcome modification requires more than risk detection — it needs proven preventive or therapeutic strategies.

Its strengths lie in its robust design, large sample size, and focus on clinically meaningful endpoints such as pre-eclampsia, fetal growth restriction, and perinatal morbidity. By randomizing women with abnormal uterine artery resistance indices, the study minimized selection bias and directly tested the clinical utility of Doppler findings rather than just their predictive accuracy. However, the trial

also has important limitations. Despite increased monitoring in the intervention arm, there was no significant reduction in maternal or perinatal morbidity and mortality, suggesting that surveillance alone may not alter the natural course of disease once abnormal placentation has occurred. The reliance on uterine artery PI >95th percentile as a screening threshold limited sensitivity, particularly for late-onset pre-eclampsia and growth restriction. Furthermore, the high false-positive rate contributed to unnecessary interventions and maternal anxiety, raising concerns about cost-effectiveness. Importantly, the trial did not incorporate prophylactic strategies such as low-dose aspirin, which have since been shown to improve outcomes in high-risk pregnancies when instituted early.

Rolnik et al. (2017) presented screening performance data from the ASPRE trial, which screened 25,797 women at 11–13 weeks using a combined algorithm of maternal characteristics, mean arterial pressure, UtA-PI, PAPP-A, and PlGF. At a 1:100 risk cut-off, detection rates were 76.7% for preterm PE and 43.1% for term PE, with a 10% screen-positive rate(3). Crucially, in the linked randomised trial, aspirin prophylaxis in high-risk women reduced the incidence of preterm PE by 62%, demonstrating that integration of UADV into a multimodal early-pregnancy screening pathway can translate into clinically meaningful prevention.

The strengths of this study are considerable. It was a large, prospective, multicentre trial with rigorous methodology, enhancing both internal and external validity. Unlike earlier single-modality studies, ASPRE provided evidence that integrated models offer superior predictive accuracy, addressing the limitations of Doppler-alone approaches. Its emphasis on *preterm* PE as an outcome also strengthened clinical relevance, since this phenotype is most strongly associated with placental dysfunction and adverse maternal–fetal outcomes.However the limitations should of the study includes the screening model, while highly effective in a trial setting, may face challenges in implementation across varied healthcare systems, especially in low -resource settings, due to the requirement for biochemical assays and trained operators for Doppler and blood pressure standardization. Moreover, while the ASPRE trial subsequently demonstrated that aspirin prophylaxis reduced the incidence of preterm PE in high-risk women, questions remain about long-term generalizability, particularly outside the specialized centres involved in the study.

Zhi et al. (2023) provided the largest quantitative synthesis to date, reviewing 41 studies up to July 2022 assessing the association between abnormal UADV and SGA across all trimesters(17). Abnormal PI/RI values and bilateral notching were consistently more common in SGA pregnancies. In the second trimester, mean PI > 95th centile was associated with approximately a threefold increased risk of SGA (OR ≈ 3), while in the third trimester, the risk rose to nearly sixfold (OR ≈ 6). Pooled mean differences in PI (+0.21) and RI (+0.05) between SGA and non-SGA pregnancies were statistically significant. The authors concluded that while UADV abnormalities are linked to SGA at any gestation, mid-pregnancy screening provides the most clinically actionable predictive information.

The strengths of this study lie in its comprehensive methodology, meta-analytic design, and inclusion of recent data, which enhance the reliability of its conclusions compared with single-centre observational studieS.Nevertheless, important limitations

remain. The included studies varied in design, population risk profiles, gestational timing of Doppler assessment, and criteria for defining SGA, leading to significant heterogeneity. This weakens the ability to generalize findings across settings. Moreover, as the authors acknowledge, SGA is an imperfect surrogate for pathological growth restriction; many constitutionally small but healthy infants may have been misclassified, which dilutes clinical applicability.

Result Summary

Collectively, these findings confirm that UADV has the highest standalone predictive accuracy for severe placental disorders when performed in the mid-trimester, but its real clinical value emerges when used within combined algorithms linked to effective interventions. First-trimester UADV alone is insufficient for universal screening but is highly informative in multimarker models, particularly for early-onset disease. Routine second-trimester UADV without an outcome-modifying pathway does not improve perinatal outcomes, but when embedded in structured risk-stratification protocols — as in the ASPRE programme — it enables actionable, preventive care. Across the eight included studies, the predictive value of uterine artery Doppler velocimetry (UADV) for placental-mediated complications showed consistent trends despite differences in gestational age at testing, thresholds, and study populations.

Mid-trimester UADV (around 20–24 weeks) emerged as the most reliable standalone screening window. In large, pragmatic cohorts such as Papageorghiou et al. (2001), mean PI above the 95th centile at 23 weeks detected 69% of PE with concomitant FGR, 24% of PE without FGR, and 13% of isolated FGR, with detection for severe early-onset cases (<32 weeks) rising to 93%. Bilateral notching gave similar sensitivity but increased false positives(1). Kurdi et al. (1998) confirmed that mid-trimester bilateral notching and elevated RI (>0.55) substantially increased the risk of PE and SGA, with the most predictive combination yielding a PPV of ~46% for major placental complications(13). García et al. (2016), in the large UTOPIA RCT, reported that mid-trimester UADV detected 59–60% of early PE/IUGR at an ~11% false-positive rate, yet disclosure of results and extra monitoring did not reduce adverse outcome rates — highlighting the difference between risk identification and outcome modification(2) (Table 3).

First-trimester UADV alone was less sensitive for broad disease detection but more informative for severe and early phenotypes. Martin et al. (2001) found that PI > 95th centile at 11–14 weeks detected only 27% of all PE but 60% of PE requiring delivery before 32 weeks, with specificity around 88% for early disease(14). Melchiorre et al. (2009) similarly showed modest overall discrimination for SGA (AUC 0.60) but better for preterm IUGR (AUC 0.78), with bilateral notching and higher RI more prevalent in affected pregnancies(15). Scandiuzzi et al. (2016) added that first-trimester RI > 95th centile was an independent predictor of hypertensive disorders (OR ~23), even if second-trimester Doppler later appeared normal — suggesting early placental maladaptation leaves a lasting risk imprint (16)(Table 3).

Meta-analytic evidence reinforced these trends: pooled data from 41 studies showed that abnormal UADV was associated with higher odds of SGA across all trimesters, with the strongest association in the third trimester (OR ≈ 6 for PI > 95th centile), followed by the second trimester (OR ≈ 3)(17).

Mean PI and RI values were significantly higher in SGA cases at all gestational stages. Integration of UADV into multimarker screening transforms its utility. Rolnik et al. (2017) in the ASPRE trial demonstrated that a first-trimester combined algorithm (maternal factors, MAP, UADV, PAPP-A, PlGF) detected 76.7% of preterm PE and 43.1% of term PE at a 10% screen-positive rate; linked randomisation to aspirin prophylaxis reduced preterm PE by 62%(3). This represents the clearest example of UADV contributing to a pathway that both identifies and successfully prevents disease (Table 3).

Ref. No.	Author & Year	GA at UADV	Doppler Criteria	Outcome(s)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Notes
1	Papageorghiou 2001 (1)	23 wks	Mean PI > 95th centile	PE + FGR	69	—	—	—	93% detection for <32 wks cases
	Papageorghiou 2001 (1)	23 wks	Mean PI > 95th centile	PE without FGR	24	—	—	—	
	Papageorghiou 2001 (1)	23 wks	Mean PI > 95th centile	Isolated FGR	13	—	—	—	
2	Martin 2001 (14)	11–14 wks	Mean PI > 95th centile (2.35)	All PE	27	—	—	—	
2	Martin 2001 (14)	11–14 wks	Mean PI > 95th centile (2.35)	Early PE (<32 wks)	60	88	—	—	
2	Martin 2001 (14)	11–14 wks	Mean PI > 95th centile (2.35)	FGR	11.7	—	—	—	
3	Kurdi 1998 (13)	20 wks	Bilateral notching + RI > 0.55	Major placental complications	—	—	46	—	OR for PE increased steeply
4	Melchiorre 2009(15)	11–14 wks	RI > 90th / 95th centile	SGA	—	—	—	—	AUC 0.60 overall; 0.78 for preterm IUGR
5	Scandiuzzi 2016(16)	11–14 wks	Mean RI > 95th centile	Hypertensive disorders	—	—	—	—	OR ~23; AUC 0.81 with maternal factors
6	Zhi 2023(17)	Various	PI > 95th centile	SGA	—	—	—	—	OR ≈ 3 (2nd tri), OR ≈ 6 (3rd tri)
7	García 2016 (UTOPIA) (2)	19–22 wks	PI > 90th centile	Early PE/ IUGR	59–60	—	—	—	FPR ~11%
8	Rolnik 2017 (ASPRE)(3)	11–13 wks	Combined algorithm (incl. UADV)	Preterm PE	76.7	—	—	—	10% screen-positive rate
8	Rolnik 2017 (ASPRE)(3)	11–13 wks	Combined algorithm (incl. UADV)	Term PE	43.1	—	—	—	

Table 3: Summary of Uterine Artery Doppler Detection Rates for Preeclampsia, Fetal Growth Restriction, and Small-for-Gestational-Age Across Eight Key Studies

Collectively, these data indicate:

- Mid-trimester UADV is the strongest single-parameter predictor for severe placental disease, particularly early-onset PE and FGR.
- First-trimester UADV has limited standalone sensitivity for all disease but detects a substantial proportion of early/severe cases and adds value in combined algorithms.

- Standalone screening without a linked intervention pathway does not improve outcomes, but integrated risk algorithms plus preventive strategies can yield measurable clinical benefit.
- Abnormalities detected early that later "normalise" should not be dismissed, as they may still signal higher residual risk.

Discussion

The synthesis of eight pivotal studies on uterine artery Doppler velocimetry (UADV) in predicting pre-eclampsia (PE), fetal growth restriction (FGR), and small for gestational age (SGA) provides a clear overview of the evolving role of this modality in obstetric risk assessment. Across the body of evidence, there is consistent agreement that abnormal uterine artery impedance, particularly elevated pulsatility index (PI), resistance index (RI), and the persistence of bilateral early diastolic notching, reflects impaired placentation and is associated with an increased likelihood of subsequent adverse pregnancy outcomes. However, the degree of predictive value, clinical applicability, and impact on outcomes is determined by multiple variables including gestational timing, integration with other risk markers, and the healthcare context in which screening is performed.

Mid-trimester UADV, especially between 19 and 24 weeks, emerges as the most reliable standalone screening window in the reviewed literature. In Papageorghiou et al. (2001), mean PI above the 95th centile at 23 weeks detected nearly 70 % of PE cases with concurrent FGR and over 90 % of the most severe early-onset cases, with acceptable false-positive rates(1). García et al. (2016) reported similar diagnostic performance in the UTOPIA trial, with approximately 60 % detection of early-onset PE and IUGR using a 90th centile threshold for mean PI(2). However, the UTOPIA trial also illustrated a critical limitation of screening in isolation: even though high-risk pregnancies were successfully identified, providing clinicians with Doppler results did not significantly improve maternal or perinatal outcomes in the absence of an effective therapeutic pathway. This finding underscores a central point for both clinical translation and policy-making—detection without intervention has limited impact.

First-trimester UADV presents a different profile of utility. Martin et al. (2001) and Melchiorre et al. (2009) demonstrated that early uterine artery abnormalities are more predictive of severe, early-onset placental disease than of all forms of PE or SGA(14,15). Martin et al. achieved 60 % detection for PE requiring delivery before 32 weeks but only 27 % for PE overall(14). Melchiorre et al. identified higher RI values and more frequent bilateral notching in pregnancies that went on to develop preterm intrauterine growth restriction, with notably better discrimination for this severe phenotype than for broader definitions of SGA(15). These results reflect the biological plausibility that early haemodynamic disturbances reflect poor placental development but may be insufficiently distinct to predict milder, late-onset disease. Importantly, both studies highlight the potential of early Doppler as part of a predictive model, rather than as a standalone screen.

The strongest evidence for such an integrated approach comes from the ASPRE trial by Rolnik et al. (2017). In this large prospective study, first-trimester UADV was incorporated into a multimodal screening algorithm alongside maternal demographic risk factors, mean arterial pressure, and biochemical markers (PAPP-A and PlGF)(3). At a

1:100 risk cut-off, the model detected 76.7 % of preterm PE cases with a 10 % false-positive rate, and crucially, high-risk women were randomised to receive aspirin prophylaxis or placebo. The intervention reduced the incidence of preterm PE by over 60 %, providing the clearest demonstration that Doppler's value is maximised when embedded in a calibrated risk model linked to a proven, outcome-modifying therapy. This study shifts the conversation from mere detection to genuine prevention and serves as a template for how screening research should be operationalised in clinical practice.

Other reviewed studies contribute unique perspectives. Kurdi et al. (1998) adopted a "one-stop" mid-trimester screening approach during the 20-week anomaly scan, combining bilateral notching and elevated RI to achieve high positive predictive values for adverse outcomes(13). However, the increased detection was accompanied by a higher false-positive rate and a dependency on operator skill, highlighting the practical trade-offs in real-world application. Scandiuzzi et al. (2016), in a smaller low-risk Brazilian cohort, showed that elevated RI in the first trimester—even if normalised later—still conferred a markedly increased risk of hypertensive disorders, suggesting that sequential Doppler evaluation could refine risk assessment and identify persistent high-risk subgroups(16). Zhi et al. (2023) provided meta-analytic evidence confirming the association between abnormal uterine artery indices and SGA across all trimesters, with the strongest odds ratios observed in mid-to-late pregnancy, reinforcing the clinical relevance of the mid-trimester as a key screening point(17).

Taken together, these studies demonstrate several overarching strengths. Many were large-scale, prospective, and often multicentre, lending strong statistical power and external validity to their findings. Doppler parameters were clearly defined and reproducible, with centile-based cut-offs facilitating standardisation. The consistent dose–response relationship between higher impedance and more severe disease lends biological credibility to the associations. Later studies, particularly ASPRE, illustrate that when Doppler is combined with other markers and linked to a proven intervention, meaningful outcome improvement is achievable.

At the same time, important limitations are evident. There is marked heterogeneity in methodologies, including differences in gestational timing, acquisition technique (transabdominal vs transvaginal), and threshold definitions, which complicates direct comparison and meta-analysis. Many earlier studies assessed Doppler at a single time point, missing the potential benefit of tracking haemodynamic changes across pregnancy. First-trimester Doppler alone has modest predictive accuracy for late-onset PE and SGA, limiting its stand-alone value in universal screening programmes. The inclusion of diverse populations remains limited, with most high-quality studies conducted in well-resourced settings; thus, extrapolation to low-resource and multi-ethnic contexts requires caution. Furthermore, in several large trials, high detection rates did not lead to improved outcomes because effective interventions were lacking or inconsistently applied.

Conclusion

In conclusion, the reviewed literature positions uterine artery Doppler as an important component of obstetric risk assessment, particularly for identifying pregnancies at risk of severe early-onset placental disease. Mid-trimester measurement offers the most robust standalone predictive performance,

while first-trimester Doppler finds its greatest value within multimodal screening models. The evidence strongly supports structured integration of Doppler into protocols that include maternal risk assessment, biochemical markers, and clearly defined management pathways. For clinical and policy adoption, the focus should shift toward models where early detection is directly linked to evidence-based interventions, thereby maximising the potential to improve maternal and perinatal outcomes. For the present thesis, these findings not only justify the use of UADV in the study design but also highlight areas for methodological refinement, such as standardised acquisition protocols, sequential Doppler assessment, and validation in diverse populations, ensuring both clinical relevance and research robustness.

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