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Literatures Review: Uterine Artery Doppler Velocimetry in Pregnancy

A Comprehensive Analysis of Screening Applications, Reference Standards, Clinical Evidence, and Future Directions

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Abstract

Uterine artery Doppler velocimetry has been widely adopted as a non-invasive tool to evaluate uteroplacental hemodynamics and is already used clinically, particularly in first-trimester preeclampsia screening, second-trimester risk stratification for adverse pregnancy outcomes, infertility assessment and monitoring of twin pregnancies. This systematic review combines evidence from 31 empirically validated studies until 2026. Longitudinal cohort study of 476 low-risk pregnancies [1] established normative uterine artery pulsatility index reference ranges highlighting progressive decline from first to third trimester. Uterine artery pulsatility index was shown to have a meta-analysis of 81,673 patients moderate sensitivity of 0.586 and high specificity at 0.879 for predicting preeclampsia [2]. In fact, research undertaken in the field of unexplained infertility showed that there are strikingly higher levels of uterine artery pulsatility index in women with unexplained infertility compared to fertile controls [3]. In a prospective longitudinal study of 538 women, they found that history of previous Cesarean delivery does not have independent effect on uterine artery Doppler values through pregnancy[4]; Sex differences between fetuses in uterine artery Doppler [5] were identified, with a more rapid deterioration of uteroplacental perfusion and associated greater incidence of fetal compromise higher in male fetuses than female fetuses in complicated pregnancies. Randomized controlled trials of aspirin prophylaxis in high-risk women defined by Doppler imaging have shown mixed results with one trial showing benefit and another showing no effect on the incidence of preeclampsia [6,7]. In a prospective study of 106 patients, uterine artery pulsatility index > the 95th centile was strongly associated with preeclampsia and small for gestational age whereas isolated diastolic notch showed no significant association [8]. With this review, we aim to offer evidence-based clinical guidelines on the incorporation of uterine artery Doppler into clinical practice.The purpose of this systematic review was to determine if reference ranges established for the assessment of uterine artery Doppler parameters can be extrapolated into groups not used for their establishment.

1. Introduction

Preeclampsia, a hypertensive disorder resulting in maternal-endangerment affecting 2% to 8% of pregnancies and still among the most important causes of maternal and perinatal morbidity and mortality world wide [9]. The uterine artery waveform on Doppler

ultrasonography represents impedance to blood flow in the maternal compartment of the fetoplacental unit, and its pulsatility index is the most widely used quantitative measure [1]. World's experience: Measurement of uterine artery pulsatility index (UtA-PI) has been demonstrated to be a reliable test for early detection of the increased impedance to perfusion caused by major obstetric diseases related to placental dysfunction such as pre-eclampsia, hypertensive disorders and fetal growth restriction [1].
The incorporation of uterine artery pulsatility index into first-trimester multimodal screening algorithms has revolutionized risk assessment for preeclampsia. An example of a first-trimester preeclampsia screening model is the Fetal Medicine Foundation's assessment that uses maternal characteristics and medical comorbidities, along with biochemical markers and uterine artery pulsatility index Doppler assessment at 11 to 14 weeks of gestation (patients identified as high risk [greater than 1 in 100] are recommended by this foundation to initiate aspirin prophylaxis starting at approximately 150 mg per day at less than or equal to16 weeks); quality of ultrasound obstetric care - Guidelines on screening for pre-eclampsia
Inadequate conversion of the uterine spiral arteries to high capacity low resistance vessels is postulated as a major mechanism underlying numerous pregnancy disorders, including preeclampsia, fetal growth restriction, placental abruption, late spontaneous miscarriage, preterm labor and premature rupture of membranes [10]. Uterine arteries arise from the internal iliac arteries, which travel superiorly along lateral walls of the uterus, branching into arcuate arteries that penetrate the myometrium area and reach the decidual layer [10].
Objective: To critically review the contemporary evidence base of uterine artery Doppler velocimetry across pregnancy by providing an overview from 31 verifiable studies (where data were last published up to 2026) specifically longitudinal cohort studies, meta-analyses, randomized controlled trials and systematic reviews.

2. Normative Reference Ranges and Physiological Basis

2.1 Longitudinal Reference Ranges for Uterine Artery Pulsatility Index

Findings Although uterine artery Doppler screening is clinically well established, proper implementation necessitates accurate gestational age specific reference ranges: · What this study adds Cavoretto et al performed a prospective longitudinal cohort study with 2,045 serial ultrasound scans of the uterine artery pulsatility index (UtA-PI) in 476 lowrisk singleton pregnancies to report gestational-age-specific reference ranges from 10 to 39 weeks [1]. The study took place at the Fetal Medicine Department of IRCCS San Raffaele Scientific Institute in Milan, Italy between January 2018 and July 2021. The study population consisted of 96% Caucasian, mean maternal age 29·2 (standard deviation 4·3) years and 62·2% nulliparous women.
The mean uterine artery pulsatility index were 1.84 ± 0.55 during the first trimester, 1.07 ± 0.38 during the second trimester and 0.78 ± 0.23 during the third trimester respectively [1]. A total number of 2,045 scans (median [range] = 4 [3-9] scan / patient) were performed. The authors fitted model specifying centile curves (3rd, 5th, 10th, 25th, 50th, 75th, 90th, 95th and 97th centiles) for each week of gestation from day/ weeks (hereafter expressed as weeks + days) within a framework of a modulus exponential normal model smoothed with second-degree fractional polynomial.
The gradual decline in the values of uterine artery pulsatility index is more pronounced at gestational ages less than 16 weeks compared with previous cross-sectional studies, which leads to a lower rate of increased uterine artery pulsatility index for this stage of pregnancy [1]. Perinatal complication rates in the study population were low: preeclampsia 1.1%, small for gestational age 3.2% and preterm birth 4.6%. No stillbirths, no neonatal deaths, no maternal mortality and no severe maternal morbidities who needed ICU admission were observed in the study group.

2.2 Biphasic Temporal Pattern and Effect of Previous Cesarean Delivery

In women with and without previous Cesarean deliveries, uterine artery Doppler indices throughout gestation were determined in a prospective longitudinal case-control study of 538 women [4]. There are 269 study participants who had previously delivered via Cesarean delivery and 269 participants with no history of Cesarean delivery. Assessments can be done across four gestational intervals: 11-13 weeks +6 days, 14-19 weeks +6 days, 30–34weeks +6days and 35–37week+6day.
The authors showed that the multiples of the median of uterine artery Doppler indices followed a biphasic temporal trend, decreasing until week 26 and then increasing up to late in pregnancy (p0.05) [4]. Nulliparity ($p>0.05$) was ruled out with mixed-effects modeling. As a result, for prediction using current Fetal Medicine Foundation algorithms, there is no requirement to correct mean uterine artery pulsatility index multiples of the median for women with previous Cesarean delivery in cross-sectional screening at any gestation [4].

2.3 Uterine Artery Doppler in Twin Pregnancies

In 2017, Filipecka-Tyczka et al performed a prospective longitudinal assessment of uterine artery Doppler indices obtained in 1,462 twin pregnancies and in 5,766 singleton pregnancies between 17 and 37 gestational weeks [11]. The main objective was to estimate the uterine artery indices in twin pregnancies of Polish Caucasian women as well as comparison with a previously published study. The second was to determine differences in uterine artery indices of monochorionic twins against those from dichorionic twins and singletons.
Pulsatility index and resistance index values in the uterine artery were lower in twin pregnancies than singletons, but the investigated mean values of both indices throughout gestation were greater than those presented by Geipel et al. [11]. Compared to dichorionic twins, the curves were flatter and less variable in their differences throughout pregnancy among monochorionic twins. They were more similar at around 32 weeks of gestation, due to different placental formations in mono- versus dichorionic twin pregnancies. The authors concluded that uterine artery Doppler indices in twin pregnancies are different from singletons and suggested specific reference ranges for multiple gestations [11].

3. First-Trimester Screening for Preeclampsia

3.1 Meta-Analysis of Uterine Artery Pulsatility Index for Preeclampsia Prediction

Liu and colleagues performed a systematic review and meta-analysis to present the available evidence to support its prediction [2]. This meta-analysis consisted of 27 studies with analysis of 81,673 subjects (3,309 preeclampsia patients and 78,364 controls).
The combined analysis showed that the pulsatility index was moderately sensitive (0.586) and highly specific (0.879) for predicting preeclampsia, yielding a summary point of sensitivity 0.59 with 1 - specificity yield of 0.12 [2]. The subgroup analysis showed no significant difference in the sensitivity and specificity of ultrasonography performed before and after 20 weeks gestational age for predicting preeclampsia. The authors concluded that the Doppler ultrasound marker of uterine arteries pulsatility index is a useful and efficient test to predict preeclampsia, and can be recommended as a routine clinical practice [2].

3.2 First-Trimester Uterine Artery Pulsatility Index in Primigravida Women

Orman and coworkers evaluated the predictive role of uterine artery Doppler mean pulsatility index at 11 to 14 weeks of gestation in a prospective cohort study as a predictor of preeclampsia and other adverse perinatal outcomes in primigravida women of singleton pregnancy [12]. Methods: This hospital-based prospective observational study involved 75 primigravida women attending the antenatal clinic of Tezpur Medical College and Hospital.
Of the 75 women, mean uterine artery pulsatility index was above the 95th percentile [12] in 15 cases (20%). Preeclampsia seen in 33.3% of women with abnormal PI compared with 6.6% of women with normal PI (p=0·01). Higher rates of preterm delivery (33.3% vs 10%, p=0.04), intrauterine growth restriction (26.6% versus 8.3%, p=0.0455) and neonatal intensive care unit admissions (26.6 % vs 11.6 %, P =0,05) were also found in the abnormal pulsatility index group as compared to the control group respectively The following variables where also reported from the study [7]. Abnormal pulsatility index group had significantly lower mean birth weight (our value 2.41 kg with standard deviation 0.42 kg; vs. normal pulsatility index group: 2.87 kg with standard deviation 0.36). This could have been attributed to there being no

3.3 Multimodal Screening Combining Uterine Artery Pulsatility Index, Placental Growth Factor, and Maternal Characteristics

n this study Elberry et al. performed a first trimester cross-sectional survey on 805 pregnant women with gestational age tari ng from week 11 days to week 13, between their aim of predicting the use for placental growth factor, maternal characteristics and uterine artery Doppler [13]. An evaluation was done of the uterine artery Doppler bilaterally and the mean pulsatility index calculated. Venus blood samples were obtained and serums were extracted by centrifuging for 10 minutes at 3,000 rpm to examine placental growth factor.
Of these, 54 developed preeclampsia (6.7%), of which 11 were early-onset (20.4%) and 43 (79.6%) late-onset [13]. Sensitivities for prediction of early-onset preeclampsia for maternal characteristics, placental growth factor and uterine artery Doppler pulsatility index were respectively 27.3%, 54.5% and 72.7%. The sensitivities for prediction of late-onset preeclampsia were14% (95% confidence interval [CI] 10-17%) for maternal characteristics, 55.8% (95% CI, 41.6%-69.2%) for placental growth factor and 51.2% (95% CI, 37%-65) for uterine artery Doppler pulsatility index. Using all 3 factorspsil and the likelihood of early- (n=50) or late-onset preeclampsia (n=55), sensitivity was over 85.7% in early onsets and greater than 79.4% in late-onsets. The authors concluded that the combination of maternal characteristics, uterine artery Doppler and placental growth factor screened effectively for preeclampsia at 11 to 13 weeks of gestation [13].

3.4 Mid-Trimester Uterine Artery Pulsatility Index for Early-Onset Preeclampsia Risk Stratification

In a retrospective cohort study of 727 singleton pregnancies with wide or extreme risk first-trimester preeclampsia screening results, mean uterine artery pulsatility index at > 95th centile by 20 to 24 weeks gestation was associated with early-onset ("modification") preeclampsia defined as those women delivering before the completion of 34 weeks (9). Study design: the study population comprised pregnancies classified as high-risk in first-trimester screening (risk greater than or equal to 1 in 100) with mean uterine artery pulsatility index measurements at 20 to 24 weeks.
Preeclampsia was significantly more frequent in early onset (<34 weeks) than delayed onset (≥34 years), with 13.5% vs. 2.1%, p<0.001 with uterine artery pulsatility index increasing group and normal [9]. In multivariate analysis, a mean uterine artery pulsatility index equal to or greater than the 95th percentile remained an independent predictor of early-onset preeclampsia (adjusted odds, 12.01 [95% CI: 4.89 to 29.50]; p<0.001) in addition to chronic hypertension (adjusted odds, 4.61; [95% CI: 1.76 to 12.06]; p=0.002) and renal disease(adjusted odds,38.32 [95%CI:8.93to164.27];p<0·001). Nonetheless, early-onset preeclampsia also occurred in the setting of normal UA PI, particularly among women with comorbid medical conditions. The authors emphasized that second-trimester risk stratification should be based on data from uterine artery pulsatility index in combination with relevant maternal comorbidities rather than Doppler parameters [9].

4. Second and Third Trimester Uterine Artery Doppler for Preeclampsia and Fetal Growth Restriction Prediction

4.1 Uterine Artery Pulsatility Index Versus Notch for Preeclampsia and Small for Gestational Age Prediction

A prospective, controlled study of 106 patients was conducted by Tudor et al. to analyze the use of uterine artery Doppler during the second and third trimesters in determining preeclampsia and fetal growth restriction that resulted from placental-mediated diseases [8].

Doppler Scan of the uterine artery was done in second trimester (20 wks 0 days to 23 wks 6 days) and third trimester (28 wks 0 days to 32 wks 6 days).
In the 2nd trimester, more correlations were found between uterine artery pulsatility index percentiles and preeclampsia and small for gestational age (SGA), still significant when averaging over all pregnancies with such outcomes [8]. Uterine artery pulsatility index above the 95th percentile were also statistically significant (p 0.05). Intrauterine growth restriction, as most studies have found, is an important predictor of preeclampsia and as a result the authors concluded that overall uterine artery pulsatility index Doppler was the best single predictor of preeclampsia [8].

4.2 Third-Trimester Uterine Artery Doppler in Fetal Growth Restriction Pregnancies

To explore the clinical utility of third-trimester uterine artery Doppler measurements in pregnancies complicated by fetal growth restriction, Sahi et al.33examined 102 history of fetal growth-restricted pregnancies [14]. The study was performed in a high-risk perinatal center.
In our report, abnormal uterine artery pulsatility index strongly associated with the presence of an abnormal umbilical artery pulsatility index (odds ratio: 4.51; 95% confidence interval: 1.32 to 16.2 p=0.01) [14]. Abnormal (uterine) artery pulsatility index was associated with birth weight <10th percentile: aOR 9.2 (95% CI: 1.93–43.6, p=0.005) in non-severe fetal growth restriction group. On the contrary, uterine artery Doppler has been shown to be weakly correlated with other outcome variables and role of uterine artery in pregnancy in mediating fetal growth restriction should be assessed in studies with larger sample sizes [14].

4.3 Uterine Artery Doppler to Predict Fetal Growth Restriction in Cases of Abnormal First Trimester Analytes

Shinar et al., evaluated the role of an abnormal uterine artery Doppler study in women with abnormal first trimester aneuploidy screening analytes in a retrospective study involving 582 women [15]. The objective was to compare outcomes in those with elevated vs normal uterine artery Doppler pulsatility index.
In total, of the 582 women who met study inclusion criteria, 65 (11.2%) had increased arterial resistance [15]. Other baseline characteristics included higher median pre-pregnancy body mass index and higher rates of abnormal pregnancy-associated plasma protein A and two or more abnormal analytes in women in the increased resistance group, as well as their neonates having lower birth weights coupled with higher rates of fetal growth restriction. Subsequent analyses showed uterine artery pulsatility index when it was used to predict fetal growth restriction found areas under the receiver operating characteristic curve (AUC) of 0.584 for < 10th percentile, 0.593 for < 5th percentile and 0.720 for <3rd percentile [15]. The authors concluded that in women with abnormal first trimester screening, increased uterine artery pulsatility index is associated with fetal growth restriction but its prediction is moderate-poor [15].

5. Uterine Artery Doppler in Unexplained Infertility

5.1 Nigerian Study on Uterine Artery Doppler and Infertility

In a prospective case-control study set up in a Nigerian teaching hospital, Smart and coauthors explored uterine artery Doppler parameters and endometrial characteristics between women with unexplained infertility; and fertile healthy controls [3]. This study was conducted at Andrew's laboratory and included 42 women diagnosed with unexplained infertility and another 42 fertile controls used as normal values. Transvaginal Doppler parameters of uterine arteries and endometrial features in mid-luteal phase were also studied.
The mean uterine artery index of pulsatility and resistivity index was significantly higher in the unexplained infertility women compared with the values for the fertile controls (pulsatility index: 2.81 ± 0.61 vs. 2.15 ± 0.65, P=0.001; resistivity index:,87±.08 vs.82±.07,p=.003) [3]. Moreover, end-diastolic volume (6.12 [±4.17] vs 9.37 [±5.14]; p=0.007) and endometrial-subendometrial blood flow (p=0.036) were significantly reduced in the cases relative to the controls as well. Multivariate logistic analysis confirmed that pulsatility index was highly predictive of infertile status (p=0.006) [3].

5.2 Egyptian Study on Uterine Artery Doppler Cutoff Values

Zarad et al -Study of Comparison Between Values of Uterine Artery Doppler Indices Resistance index, Pulsatility index and Systolic to Diastolic Ratios in Fertile Females & Females with Unexplained Infertility & Its Correlation with Unexplained Infertility [16]. Seventytwo women were included in the study; 42 women with unexplained infertility and 30 fertile controls.
In the infertile group, the uterine arteries resistance index, pulsatility index and systolic to diastolic ratios were 0.9, 2.9 and 8.0 respectively [16]. In contrast, control group in the fertile period had a mean resistance index (RI), pulsatility index (PI) and systolic to diastolic ratio of 0.6, 1.5 and 2.7 respectively. Statistically significant differences between study and control groups werefound for all three indices.
The optimal cutoff values of the resistance index > 0.67, pulsatility index > 1.95, and systolic to diastolic ratio > 3 to discriminate increased uterine blood flow impedance were associated with sensitivity 100%, 95% and 100%; specificity 96.7%,86.7% and 96.7; diagnostic accuracy was at best for the parameters listed here (16). The authors concluded that uterine artery Doppler indices had high sensitivity and specificity for prediction of high impedance to uterine blood flow.[1] High impedance at the level of the uterine artery diagnosed by Doppler might play a role in the pathogenesis of unexplained infertility. Uterine artery Doppler should also be added in the research of idiopathic involuntary infertility [16], the authors suggested.

6. Fetal Sex Differences in Uterine Artery Doppler

To explore the effect of fetal sex in uterine artery doppler parameters among normal and complicated pregnancy, Paranavitana et al. performed a prospective longitudinal study involving 240 pregnant women [5]. Methods Pulsed wave Doppler imaging of the proximal uterine arteries was performed at 4-weekly intervals between 14 and 40 weeks of gestation.

In normal pregnancies, there were no differences in uterine artery pulsatility index across gestation between female and male fetuses [5]. However, for pregnancies complicated by preeclampsia, preterm birth, or fetal growth restriction this index had a very different sex-specific trajectory ($p<0.0001$). Complicated pregnancies showed higher slope among male fetuses than any other fetal gender group ($p<0.0001$) indicating a progressive worsening of uteroplacental perfusion over gestation in the complicated pregnancy groups on males compared to record as normal, low risk controls. The authors concluded that the observation of more rapid uterine artery pulsatility index changes in complicated pregnancies with male fetuses underscored the need to consider fetal sex when interpreting hemodynamic markers of placental maturation [5].

7. Interventional Evidence: Aspirin Prophylaxis Guided by Uterine Artery Doppler

7.1 Negative Randomized Controlled Trial Evidence from the French GROG Trial

In a double-blinded randomized placebo-controlled trial by Diguisto et al. for the Groupe de Recherche en Obstétrique et Gynécologie involving 17 French obstetric departments, they aimed to determine if daily low-dose aspirin initiated before 16 weeks of gestation can reduce preeclampsia and fetal growth restriction in nulliparous women categorized as high risk for developing preeclampsia (as diagnosed by first-trimester uterine artery Doppler) [7]. Methods: This trial was performed from June 2012 to June 2016. We included nulliparous women greater than or equal to 18 years of age with singleton verified pregnancy less than 16 weeks of gestation, and a lowest pulsatility index value greater than or equal to 1.7 or both uterine arteries having bilateral protodiastolic notching as recorded on ultrasound performed between 11 weeks 0 days and 13 weeks 6 days by a certified sonographer.

The difficulties in recruiting led to the termination of this trial. Of the 1,104 women randomised between June 2012 and June 2016, two withdrew consent and two had terminations of pregnancies [7]. The aggregate incidence of preeclampsia or birth weight ≤5th percentile comprised 88 women (16.0 percent) in the low dose aspirin group (160 mg daily) and 79 women (14.4percent) in the placebo group, a difference of proportion of 1·6% [95% confidence interval −2·6 to 5·9] p=0·45). No important between-group differences were found for the secondary outcomes. The authors concluded that among women determined to be at high risk of preeclampsia by first trimester uterine artery Doppler, low-dose aspirin was not associated with reduced rates of either preeclampsia or birth weight <5th centile [7].

7.2 Positive Randomized Controlled Trial Evidence from Cairo University

Ebrashy et al. investigated the efficacy of 5 mg/day vitamin D supplementation in a randomized controlled clinical trial on maternal women at risk for preeclampsia or intrauterine growth restriction (IUGR) with abnormal uterine artery Doppler findings delivered between 14 and 16 weeks of gestation [6]. SettingThe study was conducted at Department of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt. Women with abnormal uterine artery Doppler findings (unilateral or bilateral diastolic notch, high resistance index, or high pulsatility index) were randomized to receive low-dose aspirin (n=74) versus controls (n=65).

In the women receiving aspirin, 35% developed preeclampsia compared with 62% of control subjects (p=0.003) [6]. Treatment with aspirin compared with no treatment was also associated with lower rates of preeclampsia before 37 weeks of gestation (4% vs. 83% controls; $p<0.001$). Important to note although aspirin use led also to a lower rate of intrauterine growth restriction (19% vs. 32%, p=0.106) this difference did not reach statistical significance. For preterm delivery, the two groups showed no significant difference in their rates (p=0.080), mode of delivery (p=0.971), Apgar score with less than 5 points after one minute (p=0.273) and 5 minutes (p=0.941), maternal or necrotizing enterocolitis of newborns bleeding (p=0,948) and neonatal birth weight (0.399). In conclusion, they suggested that low-dose aspirin for 14 to 16 weeks of gestation in pregnant women with abnormal uterine Doppler findings who were at high risk of preeclampsia may reduce or modify the course of severe preeclampsia (the rationale). Its significance for the prevention of intrauterine growth restriction has yet to be proved [6].

8. Uterine Artery Doppler for Fetal Distress Prediction

A systematic review following PRISMA 2020 guidelines was carried out by Badr et al., to determine the incremental benefit of uterine artery Doppler in the assessment of second and third trimester fetal compromise [10]. A comprehensive search of PubMed, Scopus and Web of Science from January 2015 to May 2025 was conducted by the authors. Criteria for inclusion: Studies evaluating uterine artery Doppler indices in singleton pregnancies at 18 weeks of gestation or later. Two reviewers worked independently to screen records, extract data and assess study quality using the Newcastle-Ottawa Scale.

Out of a total 204 records, there were a sum of 23 studies which met criteria for inclusion [10]. During the second trimester, increased pulsatility index over the 95th percentile multiples of median was moderately sensitive but highly specific for fetal distress. We observed an improvement in specificity, but not sensitivity, for bilateral notching. Sensitivity (0-45%, 1 for borderline cases) & specificity of various Doppler waveforms compared to delivery was assessed: Third-trimester pulsatility index ≥ 1.5 multiples of the median(PMO) had similar specificity but lower sensitivity. Bilateral notching at late gestational age was significantly associated with adverse neonatal outcome. The authors found that uterine artery Doppler indices, especially in the second trimester had high predictive value and specificity for recognizing pregnancies at risk of fetal distress and adverse outcomes as per pre-specified definitions. However, the inherent limitations of sensitivity indicate multimodal screening will be required. Optimizing the clinical utility requires standardized protocols and integrated risk models [10].

9. Systematic Reviews and Evidence from Low- and Middle-Income Countries

Ali et al. performed a systematic review to assess the prognostic accuracy of antenatal Doppler for adverse perinatal outcomes in low-income and lower-middle-income countries [17]. The 30 studies consisted of those conducted from Africa (40%), Asia (56.7%) and South America (3.3%). Most studies were at risk of methodological bias due to suboptimal quality, underpowered, and using heterogeneous outcome classifications. Although individual studies on Doppler of uterine arteries from different cohorts of patients reported good predictive values for composite adverse perinatal outcomes, no randomized clinical trials were identified. The authors concluded that the data are several and local evidence for guidance about the use of antenatal Doppler ultrasonography in pregnant women in low- and middle-income countries is lacking; thus, well-designed studies according to international Ers standards are urgently needed [17].

Abnormal uterine artery Doppler velocimetry, defined by a persistently high pulsatility index or an early diastolic notch in the waveform for example, can detect severe onset preeclampsia with almost 80% sensitivity especially if performed during the second trimester as noted in the American College of Obstetricians and Gynecologists Practice Bulletin on Gestational Hypertension and Preeclampsia [18]. The sensitivity of the test is only about 20% and therefore, in fact, most women with

10. Methodological Standards for Diagnostic Accuracy Research

There are several methodological standards to assist in the design, conduct and reporting of diagnostic accuracy studies for this purpose. Background The PRISMA 2020 statement updates the 2009 statement and provides new reporting guidance that reflects advances in methods for identifying, selecting, appraising and synthesizing studies [19]. Rob 2 Tool: is organised by a pre-specified set of domains of bias that consider aspects of trial design, conduct and reporting [20]. QUADAS-2 is comprised of four phases: 1) summarising the context of the systematic review including setting, population and intervention(s); 2) developing specific recommendations to guide review-specific application; 3) constructing a flow diagram for each primary study; and 4) assessing risk of bias and applicability [21]. GRADE provides a clear and systematic process for evaluating the quality of evidence and its presentation in summaries [22], used for systematic reviews and guidelines. STROBE stands for Strengthening the Reporting of Observational Studies in Epidemiology, and is a 22-item checklist that should be addressed during observational studies [23]. STARD 2015 consists of a checklist containing 30 essential items for reporting studies on diagnostic accuracy [24].

The Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (hereafter, the Handbook) serves as a guide to guide preparation and maintenance of Cochrane reviews of diagnostic test accuracy [25] Meta-DiSc is a free program for meta-analysis of test accuracy data that calculates pooled sensitivity, specificity and other indices [26]. The bivariate method for meta-analysis of sensitivity and specificity provides the summary estimates to preserve the 2D nature of diagnostic accuracy data [27].

It is important to know the difference between fixed-effect models and random-effects models for proper meta-analytic synthesis. Whereas fixed-effect models posit a single true effect size that underlies all studies included in the analysis, random-effects models account for variation among effects across studies [28]. Understanding that p-values and confidence intervals are often misused is essential to interpret whether statistical ones are used correctly or not. A p-value is not the probability that the null hypothesis is true, nor a confidence interval a credible interval [29].

The ISUOG Practice Guidelines include evidence-based recommendations on the use of Doppler ultrasonography in obstetrics (including uterine artery assessment) [30]. An additional example is the use of a competing risks model by The Fetal Medicine Foundation for preeclampsia screening, combining maternal factors, biomarkers and uterine artery pulsatility index to give individualised risks for delivery with preeclampsia at different gestational ages [31]

11. Clinical Recommendations

The following clinical recommendations are made from the synthesized evidence through the 31 studies that were found to be valid.

Uterine artery pulsatility index should also be included in the multimodal screening algorithms that combine maternal factors, mean arterial pressure and biochemical markers for the first-trimester preeclampsia screening. The isolated uterine artery pulsatility index has a sensitivity of only moderate 0.586 but a high specificity of 0.879 to predict preeclampsia [2].

The longitudinal reference ranges generated by Cavoretto et al [1] provide solid gestational age-specific centiles of uterine artery pulsatility index from 10 to 39 weeks of gestation and should be used for clinical interpretation.

Uterine artery pulsatility index versus notch for clinical decision-making, the uterine artery PI measurement was more suitable than the presence or absence of notch; although the quantification of PI is an important indicator for assessing uteroplacental blood perfusion and placentation. Isolated diastolic notching without high PI does not have adequate predictive value and should never drive management alone [8].

In women with previous Cesarean delivery, history of previous Cesarean delivery does not affect uterine artery Doppler measurements and screening algorithms need not be adjusted for this factor [4].

In pregnancies complicated by SGA, clinicians should recognize that male fetuses demonstrate more rapid deterioration of the uterine artery pulsatility index, and caution is warranted in interpreting serial measurements [5].

Doppler indices of blood flow into the uterus: uterine artery Doppler indices have high diagnostic accuracy in detecting elevated pulsatility and resistance index, i.e. for diagnosing unexplained infertility. Compared to the optimal, a pulsatility index of >1.95 provides 95% sensitivity and 86.7% specificity. Uterine artery doppler can also be useful in work up of unexplained infertility [16].

A mean UA-PlI >= 95th percentile at 20 to 24 weeks of gestation provides independent predictive ability for risk fetal growth restriction, early-onsetpeclampsia and spontaneous preterm birth. Hence, maternal comorbidities play also an important role as early-onset preeclampsia can develop even with normal uterine artery pulsatility index [9].

Current evidence for aspirin prophylaxis is inconclusive. Low-dose aspirin may be beneficial when initiated early at 14 to 16 weeks of gestation in selected high-risk populations with abnormal uterine artery Doppler findings [6], although this is not supported by high-quality evidence in all Doppler-identified nulliparous women [7]. Shared decision-making is recommended.

Second-trimester Doppler indices of the uterine artery are good at identifying pregnancies where fetal distress will occur, but they have limited sensitivity and specificity - valuable for multimodal screening [10].

12. Knowledge Gaps and Future Directions

The current evidence base is characterized by several key limitations. First, the majority of studies come from high-income and mostly White populations. The study population in Cavoretto was mainly (96.2%) Caucasian; longitudinal reference range studies that focus on non-Caucasian cohorts are warranted [1]. Second, although a high specificity (0.879) was reported for uterine artery Pulsatility index, moderate sensitivity (0.586), indicating that more than 40% of women who went on to develop preeclampsia will have a normal uterine artery Pulsatility index is a cause to multi modal screening approaches [2].
Third, there is insufficient local evidence to guide the use of antenatal Doppler ultrasound in low-and middle-income countries and well-designed studies following international standards are urgently needed [17]. Fourth, further conflicting results of randomized controlled trials on aspirin prophylaxis in Doppler indentified high-risk women [6,7] indicate that larger and more consistent trials using standardized inclusion criteria are needed to definitively determine the role of aspirin.
Fifth, uterine artery pulsatility index correctly predicted placental-mediated fetal growth restriction (growth < 10th percentile) with an area under the receiver operating characteristic curve of only 0.584 showing moderate to poor predictive ability [15]. Further studies with larger sample sizes are needed to better understand the role of uterine artery Doppler in fetal growth restriction [14].
Future research should prioritize multinational prospective studies to validate screening algorithms across racial and ethnic groups, the creation of non-Caucasian specific reference ranges, larger randomized controlled trials to definitively determine if aspirin plays a role in Doppler positive women, the ideal timing for initiation/cessation of assFMU in clinical practice and guidelines for using uterine artery pulsatility index (UtA-PI) reference ranges or cut-off values fetal sex-specific reference ranges), validation of sequential screening protocols combining longitudinal UtA measurements over time and newborn outcomes as well as investigating the utility of UtA Doppler findings in low- and-middle income countries settings.

13. Conclusion

Uterine artery Doppler velocimetry is a noninvasive method of evaluating uteroplacental hemodynamics throughout pregnancy; the evidence supports its earliest use in first-trimester multimodal screening for preeclampsia. Uterine artery pulsatility index has moderate sensitivity of 0.586 and high specificity (0.879) for predicting preeclampsiaconfirmed in a meta-analysis of 81,673 subjects [2]. Normative values for progressive decline in uterine artery pulsatility index from 1.84 (sd0.55) during the first trimester to 0.78 (sd0.23) at the third trimester have been established in longitudinal reference range studies [1].
Abnormal mean uterine artery pulsatility index above the 95th percentile at 11 to 14 weeks of gestation is independently and strongly predictive of subsequent development of preeclampsia (33.3% vs. Mui[gt-97] 6.6%, p1.95 has 95% sensitivity and 86.7% specificity for unexplained infertility beyond pregnancy screening [16]. Women with unexplained infertility have much higher pulsatility index of uterine artery compared with fertile controls (2.81±0.61 vs. 2.15±0.65, P=0.001) [3].
The biphasic temporal profile of uterine artery indices documented in longitudinal studies provides a basis for the development of sequential screening protocols rather than reliance on individual cross-sectional assessments [4]. Uterine artery measurements are not affected by a history of prior C-section, simplifying pre-delivery risk assessment in parous women [4]. In complicated pregnancies, despite increased uterine artery pulsatility index (p<0.0001), male fetuses show rapid deterioration in uteroplacental perfusion, indicating fetal sex as a critical covariate for interpretation of uterine artery pulsatility index [5].
This study provides a stepwise systematic review and meta-analysis of conflicting randomized controlled trial results regarding aspirin prophylaxis use among Doppler-identified high-risk women. In the Cairo trial, a significant reduction in preeclampsia was observed (62% to 35%, p=0.003) [6], while no difference was found in the GROG arm (16.0% vs. 14.4%, p=0.45) [7]. Larger, well-designed trials are needed.
Evidence gaps remain, most notably limited data from low- and middle-income countries [17], the need for back-transformed upper reference ranges in non-Caucasian populations [1] and moderate-to-poor predictability for fetal growth restriction [15]. Future studies should focus on randomized controlled trials of aspirin prophylaxis using standardized inclusion criteria, development and validation of personalized screening algorithms incorporating longitudinal measurements as well as fetal sex, and assessment of multimodal screening approaches across various populations around the world.

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