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REVIEW ARTICLE

Uterine artery Doppler: Changing Concepts in Prediction and Prevention of PE and FGR

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Abstract One of the most promising screening tools in detection of PE and FGR is uterine artery Doppler velocimetry. The underlying pathology for the development of PE is thought to be due to defective trophoblastic invasion of uterine spiral arteries. Increased impedance during mid-trimester is known to be associated with a high incidence of adverse pregnancy outcomes. High resistance in uterine arteries can be observed as early in the first trimester in cases with impaired placentation. The predictive efficacy of first trimester UtA Doppler has improved after the development of risk specific algorithm by including maternal characteristics, biophysical and biochemical parameters. With the understanding of late onset FGR and PE, it was realised that first trimester UtA Doppler may not serve as an efficient marker to identify this group which led to the evolution of its assessment in third trimester. The importance of UtA Doppler in third trimester is its ability to differentiate a physiologically small baby from a pathologically small fetus, which is growth restricted. PE and FGR remains an important cause of maternal and fetal mortality and its prediction is a challenging task which needs to be done early in gestation. Low dose aspirin when started before 16 weeks in the truly high risk population has proven to significantly reduce PE and FGR. To initiate aspirin therapy, the development of first trimester risk prediction model remains the key component. This paper is a review of the predictive efficacy of UtA Doppler in detecting uteroplacental insufficiency in each of the three trimesters.

Keywords Screening · Preeclampsia · FGR · Uterine artery Doppler · Pulsatility index · Sensitivity

Abbreviations

PE	Pre-eclampsia
FGR	Fetal growth restriction
UtA	Uterine artery
PAPP-A	Pregnancy associated placental protein A
MAP	Mean arterial pressure
SGA	Small for gestational age
AGA	Appropriate for gestational age
EFW	Expected fetal weight
FPR	False positive rate
RI	Resistance index
PI	Pulsatility index
FMF	Fetal medicine foundation
MCA	Middle cerebral artery
CPR	Cerebroplacental ratio
PLGF	Placental growth factors
CLASP	Collaborative low-dose aspirin study in pregnancy
ASPRE	Aspirin for evidence-based preeclampsia prevention
NICE	National Institute for Health and Care Excellence
WHO	World Health Organisation

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Introduction

Pre-eclampsia and intrauterine growth restriction still remains as one of the major causes of maternal and perinatal morbidity and mortality. Accurate prediction of PE and FGR is essential for the initiation of preventive therapy and this also aids in targeting the group which would need increased antenatal surveillance. Extensive research over the past 35 years has evaluated the use of UtA Doppler for prediction of PE and FGR in mid trimester [1–5]. However, the sensitivity of the test and the recommendations for using it as a routine screening tool are highly inconclusive [6, 7]. Few studies recommend UtA Doppler screening only in the high risk group and have observed an increased risk of adverse pregnancy outcomes in that group [4, 8].

From 1997 onwards, researchers focussed on changes in UtA Doppler for early prediction of PE and FGR in 11–14 week scan [9, 10]. This later evolved into a multiparametric testing, that combined UtA Doppler with biophysical and biochemical parameters which increased the sensitivity of the test [11–14]. As evidence poured in for the benefits of low dose aspirin started early in gestation, the focus of UtA Doppler has been shifted from mid to first trimester paving the way for both prediction and prevention of PE and FGR [15–17]. There is rising evidence that prediction of adverse pregnancy outcomes in SGA foetuses can be influenced by assessment of third trimester UtA Doppler [18–20]. The authors review the changing concept of UtA Doppler assessment in the prediction and prevention of uteroplacental insufficiency.

Pathophysiology

The underlying mechanism of early onset or placental PE is identified to be impaired trophoblastic invasion of the maternal spiral arteries and their conversion from narrow vessel to wide non-muscular channels. The uteroplacental circulation remains in a state of high resistance in cases with defective trophoblastic invasion which can be measured noninvasively by UtA Doppler ultrasound as early as in first trimester [21]. Impaired trophoblastic invasion leads to defective perfusion of placenta causing placental ischemia and release of inflammatory factors causing endothelial dysfunction and platelet aggregation. Evidence exist on decreased uterine artery blood flow volume in cases with high uterine PI irrespective of whether the fetus is growth restricted or appropriate for gestational age [22].

The impedance is increased in early onset PE and FGR and predates the onset of the clinical symptoms by several weeks. Early onset forms of PE and FGR are due to disorders of deep placentation whereas late onset PE or maternal PE is hypothesised to be due to secondary maternal response to endothelial dysfunction and has a heterogenous etiology [23, 24]. In late onset PE, placenta may be normal reflecting that UtA Doppler may not be affected in all cases. The association of a bimodal birthweight distribution with late-onset PE supports the concept of two different etiologies one which is early-onset PE with high uterine impedance and SGA births, and the other late-onset PE with normal mid-gestational uterine flow related to good trophoblast development and more of AGA births [25]. This explains that first trimester UtA Doppler may not serve as an effective predictor in late onset PE or maternal PE.

Objective Assessment of UtA Doppler

The criteria to define an abnormal UtA Doppler varied between studies, the concept of notching which had been used extensively in the past is very subjective and Doppler indices serve as a better means of uniform reporting. Jeltsje et al. in his review concluded that a pulsatility index, alone or combined with notching, is the most predictive Doppler index and that PI should be used in clinical practice [26]. Normograms for mean uterine artery PI between 11 and 41 weeks (Table 1) has been established by Gomez et al. and it serves as the reference standard for UtA Doppler assessment [27].

Unilateral or bilateral or placental side Doppler which to be measured had been evaluated and few authors rely more on placental side Doppler [28, 29]. The idea behind this is based on the assumption that impedance to flow in the uterine arteries is lower on the side of implantation, and hence the lower uterine PI should more accurately reflect the true extent of trophoblastic invasion [30]. However it has also been observed that the differences that exist between the lower, mean and higher uterine artery PI are unlikely to have a significant impact on the screening sensitivity [31]. Thus mean uterine artery PI would serve as a standard methodology for reporting uterine artery Doppler.

Mid Trimester UtA Doppler

The sensitivity and specificity of mid trimester UtA Doppler assessment have been analysed over the past decades with promising results. It has been uniformly agreed that, high resistance flow in UtA Doppler during mid-trimester is associated with increased incidence of adverse perinatal outcomes [32–35]. Table 2 is an illustration of various studies evaluating the predictive efficacy of UtA Doppler

Table 1 Normogram for UtA-PI between 11 and 41 weeks of gestation (Reproduction from Gomez et al. [27])

GA (weeks)	5th centile	50th centile	95th centile
11	1.18	1.79	2.70
12	1.11	1.68	2.53
13	1.05	1.58	2.38
14	0.99	1.49	2.24
15	0.94	1.41	2.11
16	0.89	1.33	1.99
17	0.85	1.27	1.88
18	0.81	1.20	1.79
19	0.78	1.15	1.70
20	0.74	1.10	1.61
21	0.71	1.05	1.54
22	0.69	1.00	1.47
23	0.66	0.96	1.41
24	0.64	0.93	1.35
25	0.62	0.89	1.30
26	0.60	0.86	1.25
27	0.58	0.84	1.21
28	0.56	0.81	1.17
29	0.55	0.79	1.13
30	0.54	0.77	1.10
31	0.52	0.75	1.06
32	0.51	0.73	1.04
33	0.50	0.71	1.01
34	0.50	0.70	0.99
35	0.49	0.69	0.97
36	0.48	0.68	0.95
37	0.48	0.67	0.94
38	0.47	0.66	0.92
39	0.47	0.65	0.91
40	0.47	0.65	0.90
41	0.47	0.65	0.89

in mid-trimester. Women with normal uterine artery Doppler results are unlikely to develop early onset PE and FGR [45]. The recent study in 2016 by Garcia et al. concluded that routine mid trimester UtA Doppler identifies approximately 60% of women at risk for placental complications. However, they also concluded that targeting the screen positive group for increased surveillance does not improve maternal and perinatal outcomes [46].

First Trimester UtA Doppler

There is increasing evidence regarding the effectiveness of first trimester UtA Doppler in assessing uteroplacental insufficiency [47, 48]. Table 3 is a review of studies which evaluated uterine artery Doppler in first trimester. Velauthar et al. in their meta-analysis reviewed the accuracy of uterine artery Doppler analysis in first trimester and as per their study the sensitivity of UtA PI for detection of early onset PE is around 47%, for any PE it is 26% and for early onset FGR it is 39%, FGR at any gestational age it is 15%. UtA Doppler PI alone in first trimester may not serve as an efficient marker [12, 15]. Therefore, there evolved the need for multiparametric testing and various studies quote that the performance of screening can be improved by combining UtA Doppler with maternal characteristics and biochemical testing.

Multiparametric Approach in First Trimester

In chromosomally normal pregnancies, there is evidence that low maternal serum PAPP-A and PLGF are associated with increased risk for subsequent development of PE and FGR. It has also been studied that preeclamptic women tend to have subtle increase in MAP well before the onset of clinical symptoms. Poon and Akolekar et al. in their study had emphasized that the inclusion of maternal characteristics, UtA PI, MAP and biochemical testing at 11–13 weeks of gestation improves the predictive efficacy of PE screening [11, 52]. Table 4 illustrates the efficacy of first trimester uterine artery Doppler when combined with these parameters.

Third Trimester UtA Doppler

High UtA PI in the third trimester can be an independent phenomenon or it can be persistence of the abnormal waveforms detected early in gestation [56]. Table 5 is an illustration of two studies which lay emphasis on the role of third trimester UtA Doppler in diagnosing late onset FGR and PE. For almost 20 years, the umbilical artery (UA) has been widely accepted as the standard to identify FGR. Umbilical Artery Doppler can identify severe placental disease but it fails to pick up mild placental insufficiency which constitute a proportion of early-onset cases and virtually all instances of late-onset FGR. Hence late-onset SGA foetuses with normal umbilical artery Doppler velocimetry may have true growth restriction and are at an increased risk for adverse perinatal outcome [60, 61].

Third trimester UtA PI in association with an EFW $<$ 3rd centile, CPR $<$ 5th centile and MCA pulsatility index $<$ 5th centile was used as a diagnostic handle in staging pathologically growth restricted fetus [62]. Severi et al. opined that foetuses with abnormal MCA Dopplers and high UtA Doppler have an exceedingly high risk (86%) of developing distress whereas when both these waveforms

Table 2 Illustration of various studies utilising second trimester uterine artery Doppler for prediction of PE and FGR

References	Methodology and markers uterine artery Doppler	Population	DR for FPR 5/10%		Sensitivity		Specificity		Positive predictive value (PPV)		Negative predictive value (NPV)	
			PE	FGR	PE (A)	FGR/ SGA	PE (A)	FGR/ SGA	PE (A)	FGR/ SGA	PE	FGR/ SGA
Arduini et al. [36]	*At 18–20 weeks*	60 HRP			63.6		84.2		70		80	
	RI > 0.57											
North et al. [28]	*At 19–24 weeks*	458 Primi			(1) 27	(1) 50	(1) 89	(1) 90	(1) 8	(1) 27	(1) 97	(1) 91
	(1) Placental side RI > 90 %				(2) 53	(2) 47	(2) 88	(2) 89	(2) 14	(2) 23	(2) 98	(2) 96
	(2) Placental side S/D ratio > 90%											
Valensise et al. [37]	*At 22 weeks*	272 Primi			88	66	93	95	30	53	99	97
	RI > 0.58											
Kurdi et al. [38]	*At 19–21 weeks*	946 Routine			61.9	36.8	88.7	89.2	11.1	17.9	99.0	95.7
	B notches with mean RI > 0.55/U notch and mean RI > 0.65/mean RI > 0.7											
Coleman et al. [39]	*At 22–24 weeks*	116 HRP			(1) 91	(1) 84	(1) 42	(1) 39	(1) 37	(1) 33	(1) 92	(1) 87
	(1) U/B RI > 0.58				(2) 63	(2) 61	(2) 71	(2) 69	(2) 49	(2) 44	(2) 81	(2) 81
	(2) Any notch				(3) 63	(3) 61	(3) 72	(3) 70	(3) 50	(3) 45	(3) 82	(3) 82
	(3) RI > 0.58 and notch											
Papageorghiou et al. [40]	*At 23 weeks*	7851 Routine			(1) 23.9	(1) 13.2	(1) 95.1	(1) 95.7	(1) 4.2	(1) 22.9	(1) 99.3	(1) 91.8
	(1) Mean PI >1.63 in 401				(2) 25.4	(2) 19.9	(2) 90.9	(2) 91.8	(2) 2.5	(2) 19.1	(2) 99.3	(2) 92.2
	(2) B notches in 728				(3) 40.8	(3) 24.4	(3) 88.4	(3) 89.3	(3) 3.1	(3) 18.2	(3) 99.4	(3) 92.4
	(3) Mean PI >1.63 or B notches in 932											
Harrington et al. [41]	*At 20 weeks*	628 Multipara			(1) 95	(1) 42	(1) 80	(1) 80	(1) 38.8	(1) 42	(1) 99.2	(1) 95.9
	Mean RI > 0.55 + B notches/mean RI > 0.65 + U notch	(1) HRP 170 (2) LRP 458			(2) 50	(2) 34.8	(2) 91.2	(2) 92.4	(2) 2.1	(2) 19.5	(2) 99.8	(2) 96.4
Spencer et al. [42]	*At 22–24 weeks*	4390 Routine	(1) 54.7									
	(1) Mean PI		(2) 62.1									
	(2) Serum PAPP-A, Free bHCG at 11–13 weeks + mean PI											

Table 2 continued

References	Methodology and markers uterine artery Doppler	Population	DR for FPR 5/10%		Sensitivity		Specificity		Positive predictive value (PPV)		Negative predictive value (NPV)	
			PE	FGR	PE (A)	FGR/ SGA	PE (A)	FGR/ SGA	PE (A)	FGR/ SGA	PE	FGR/ SGA
Onwudiwe et al. [43]	*At 22–24 weeks* (1) Mean PI (2) PI + MAP + maternal characteristics	3529 Routine	(1) E—95.7 L—41.0 (2) E—100 L—56.4	22.3 27.3								
Yu et al. [44]	*At 22–24 weeks* Mean PI > 95 %	30369 Routine	E—77 L—22									
Pongrojpaw et al. [45]	*At 20–24 weeks* (1) PI > 1.58 (2) Any notch (3) PI + notch	330 HRP			(1) 81.48 (2) 62.96 (3) 59.25	(1) 81.25 (2) 56.25 (3) 56.25	(1) 48.84 (2) 65.34 (3) 66.67	(1) 47.77 (2) 64.0 (3) 65.60	(1) 12.42 (2) 13.43 (3) 13.67	(1) 7.34 (2) 7.37 (3) 7.69	(1) 96.73 (2) 95.19 (3) 94.83	(1) 98.00 (2) 96.63 (3) 96.73

DR detection rate, *FPR* false positive rate, *UtA* uterine artery Doppler, *S/D ratio* systolic/diastolic ratio, *U/B notches* unilateral/bilateral notches, *RI* resistance index, *PI* pulsatility index, *HRP* high risk population, *LRP* low risk population, *MAP* mean arterial pressure, *PAPP-A* pregnancy associated plasma protein-A, *Beta HCG* beta human chorionic gonadotrophin, *E* early, *L* late, *A* any, *PE* pre-eclampsia, *FGR* fetal growth restriction, *SGA* small for gestation age

Table 3 Illustration of studies done at 11–14 weeks using uterine artery Doppler alone

References	Methodology and markers uterine artery Doppler	Population	Sensitivity			Specificity		Positive predictive value (PPV)		Negative predictive value (NPV)	
			PE		FGR/SGA	PE	FGR/SGA	PE	FGR/SGA	PE	FGR/SGA
			E	A				A	A	A	A
Martin et al. [49]	Mean PI > 95% (2.35)	3045 Routine		27.0	11.7	95.4	95.6	11.0	21.9	98.4	91.1
Gomez et al. [12]	Mean PI > 95% + B-notch	999 Routine		24	24.3	95.1	95.4	11.3	16.9	97.9	97
Pilalis et al. [50]	Mean PI > 95%	1123 Routine		21.1	17.8						
Melchiorre et al. [51]	(1) RI > 90%	3058 Routine	(1) 48.5		(1) 91.8			(1) 6.2		(1) 99.4	
Martin et al. [49]	(2) RI > 95%		(2) 24.2		(2) 95.8			(2) 6.0		(2) 99.1	
Gomez et al. [12]	(3) RI > 97.5%		(3) 12.1		(3) 98.1			(3) 6.7		(3) 99.0	
	(4) B-notch		(4) 75.8		(4) 55.3			(4) 1.9		(4) 9.5	
Pilalis et al. [50]	RI or PI > 90% + U/B-notch	55974 LRP	47.8	26.4	E—39.2 A—15.4	E—92.1 A—93.4	E—93.1 A—93.3				

E early, *A* any, *PE* pre-eclampsia, *FGR* fetal growth restriction, *SGA* small for gestation age, *UtA* uterine artery Doppler, *RI* resistance index, *PI* pulsatility index, *U/B notches* unilateral/bilateral notches, *LRP* low risk pregnancy

are normal the chances of developing distress is minimal (4%) [63]. The utility of third trimester UtA Doppler is that it identifies that subset of fetus who are at high risk of developing neurological compromise and also women who would develop late onset PE. Various algorithms combining third trimester UtA PI with biochemical parameters to predict late onset PE are under research [64].

Sequential Screening

The role of sequential screening is based on the observation that persistence of high resistance waveforms throughout pregnancy have an increased efficacy in predicting PE and FGR [65–72]. Table 6 is an illustration of various studies in sequential screening in various trimesters. Gomez et al. [65] opined that women in whom mean UtA PI shifted from abnormal to normal between two trimesters and women in whom the reverse shift occurs showed a similar risk for adverse outcomes. On the contrary, few others conclude that, there was a significant rise in the rate of adverse pregnancy outcomes in the group which had persistent increased resistance in the 3rd trimester (43.8%) compared to those who had normal flow pattern (6.8%) [73].

Importance of Screening

PE is responsible for approximately 50,000 maternal deaths annually and is a leading cause of perinatal morbidity and mortality. Many studies quote about 15–18% of maternal mortality to be associated with PE. One in six babies born to pre-eclamptic mother is often preterm or severely growth restricted. Neonatal morbidity and mortality is approximately 7–9% in pregnancies complicated with PE. Recent studies have established the benefits of using low-dose aspirin early in gestation in high risk population to reduce the incidence of PE and FGR [17, 78, 79]. CLASP trail concluded that there is no role for routine usage of aspirin in all women but it may be beneficial in the high risk group [80]. When treatment was initiated at or before 16 weeks of gestation, the risk of perinatal death was reduced by about 60%, whereas when started after 16 weeks, there was no significant effect [16]. This finding is compatible with the hypothesis that aspirin improves the transformation of uterine spiral arteries and decreases disorders of deep placentation, which is a major cause of perinatal death.

Table 4 Illustration of studies at 11–14 weeks using combined algorithm for prediction of PE and FGR

References	Methodology and markers uterine artery Doppler	Population	DR/FPR—5/10%	
			PE	FGR/SGA
Nicolaides et al. [53]	(1) Median PI	433 Routine	(1) 40	
	(2) Median PI + PP-13		(2) 90	
Plasencia et al. [54]	(1) Mean PI alone	6015 Routine	(1) E—81.8 L—30.6	(1) 18.4
	(2) Combined (mean PI, bHCG, PAPP-A + maternal factors)		(2) E—81.8 L—51.8	(2) 24.6
Poon et al. [30]	(1) Maternal risk factors + L-PI	8366 Routine	(1) E—81.1 L—45.3	
	(2) Maternal risk factors + L-PI + MAP		(2) E—89.2 L—57.0	
Poon et al. [11]	(1) L-PI + MAP	8366 Routine	(1) E—87.5 L—57.0	
	(2) L-PI + MAP + biochemical markers(PIGF, PAPP-A, and others)		(2) E—92.3 L—65.6	
Audibert et al. [55]	UtA + maternal characteristics + serum biomarkers	893 Primi	E—75	
Akolekar et al. [52]	(1) Maternal factors + PI	(752 affected + 32850 unaffected)	(1) E—54.1 I—36.9 L—27.1	
	(2) Maternal factors + biophysical + other biochemical markers		(2) E—91.0 I—79.4 L—60.9	

E early, *I* intermediate, *L* late, *PE* pre-eclampsia, *FGR* fetal growth restriction, *SGA* small for gestation age, *UtA* uterine artery Doppler, *RI* resistance index, *PI* pulsatility index, *U/B notches* unilateral/bilateral notches, *L-PI* lowest-pulsatility index, *PAPP-A* pregnancy associated plasma protein-A, *Beta HCG* beta human chorionic gonadotrophin, *PP-13* placental protein 13, *FPR* false positive ratio, *DR* detection rate, *MAP* mean arterial pressure

Table 5 Illustration of various studies using uterine artery Doppler in third trimester for prediction of PE and FGR

References	Methodology and markers uterine artery Doppler	Population	DR /FPR 5 or 10%	Sensitivity	Specificity	Positive predictive value (PPV)	Negative predictive value (NPV)
			PE		Adverse outcomes		
Lai et al. [57]	*At 30–33 weeks* (1) UtA PI (2) UtA PI + maternal history	4294 Routine	FPR 10% (1) I—43.2 L—26.9 (2) I—70.3 L—54.6				
Rai et al. [58]	*At 28–37 weeks* UtA PI > 1.2 + notch/umbilical artery PI > 2 SD, absence or reversal of end diastolic flow	66 HRP	86		81	93	68
Tsiakkas et al. [59]	*At 30–34 weeks* UtA PI + MAP + PLGF + sFLt-1	7927 Routine	FPR 5% Preterm PE 98% Term PE 49%				

UtA Doppler uterine Doppler, *S/D ratio* systolic/diastolic ratio, *U/B notches* unilateral/bilateral notches, *RI* resistance index, *PI* pulsatility index, *PE* preeclampsia, *HRP* high risk population, *MAP* mean arterial pressure, *I* intermediate, *L* late, *DR* detection rate, *PLGF* placental growth factors, *sFLt 1* serum soluble Fms-Like Tyrosine Kinase-1

Ideal Screening Test

An ideal screening test should be simple, non-invasive, inexpensive, easily available, reproducible and must have the option of being done in early pregnancy to allow for effective preventive therapy. After the onset of aneuploidy screening, the 11–14 weeks scan is now a part of routine antenatal care and hence, performing screening for uteroplacental insufficiency in this period is ideal [81]. As there is no preventive role of aspirin when started in mid trimester, routine assessment of UtA Doppler in mid-trimester fails as a screening tool [82, 83]. Preeclampsia has a heterogenous etiology which cannot be attributed to placental cause alone and hence uterine artery Doppler assessment alone may not suffice in PE prediction. The cardiovascular, metabolic and prothrombotic risk profile of the woman with a previous history of preeclampsia or a nulliparous woman needs to be incorporated in risk assessment [84–86].

Whom to Screen

If screening would be confined only to high risk women e.g. with a previous history of PE then we would miss low-risk nulliparous women in whom majority of cases of preeclampsia occur [87]. The usage of patient specific risk algorithm model gave a better prediction of risk than those established by NICE guidelines or by UtA Doppler assessment alone in first trimester [88]. Hence individual uterine artery PI to be replaced by MoM values in risk assessment including the variables from maternal characteristics and history [89–94]. Effective first trimester screening for PE and FGR could be done with the combined use of specific algorithm and a detection rate of 95% can be achieved with a FPR of 10% [92, 95]. The results of ASPRE trial emphasises the usage of FMF algorithm in prediction of PE and the benefits of aspirin in the high risk group [89].

Based on emerging evidences from literatures and from our data we would like to conclude that first trimester screening for PE and FGR should be universal [96, 97]. The risk algorithm claims to have a high negative predictive value if applied to general population [98]. This test would also help in triaging the screen positive women, who can then be started on aspirin and subjected to increased antenatal surveillance. When PAPP-A was combined with uterine PI, MAP, and maternal characteristics, the predictive efficacy in screening for FGR was fairly good [52]. A major purpose of prenatal care is to detect incipient preeclampsia and to prevent its progression which can be achieved by implementing first trimester screening for all [86]. Abnormal UtA Doppler in third trimester identifies foetuses which are pathologically growth restricted and those women who are at high risk of developing PE in late trimester. This aids in early and prompt referral to tertiary care centre for institutional delivery under expert care [99, 100].

Table 6 Illustration of various studies which used sequential screening for prediction of PE and FGR

References	Methodology and markers uterine artery Doppler	Population	Sequential screening	Sensitivity		Specificity		Positive predictive value (PPV)		Negative predictive value (NPV)	
				PE	FGR/SGA	PE	FGR/SGA	PE	FGR/SGA	PE	FGR/SGA
Harrington [67]	B Notches	1326 Routine	19–21 and 24 wks	81.2	57.6			27	31.2		
Ashraf Jamal et al. [73]	Mean PI > 95% + U/B-notch	435	18–24 and 30–34 wks	30.4	47.1	90.5	90.9	15.2	17.4	95.9	97.7
		134 Routine		S—50		S—90.5		S—13.0		S—98.5	
Steel [74]	Abnormal wave forms	1014 Primi	18 and 24 wks	63	100						
Frusca et al. [75]	Mean RI > 0.58 + U/B notches	419 Primi	20 and 24 wks	50	43						
Myatt et al. [76]	(1) RI/PI > 75%	2188 LRP	16 and 24 wks	(1) 43		(1) 67		(1) 10		(1) 93	
	(2) RI/PI > 75% + U/B notch			(2) E–78 S—53		(2) E—66 S—66		(2) E—1.9 S—5		(2) E—99.7 S—98	
Afrakhteh et al. [77]	PI + RI + B-Notch	205 Routine	15–20	(1) 77.2		(1) 89.6		(1) 47.2		(1) 97.0	
	(1) Mean RI > 95%			(2) 48.8		(2) 90.7		(2) 58.0		(2) 86.9	
	(2) Mean PI > 95%			(3) 36.1		(3) 97.0		(3) 72.2		(3) 87.7	
	(3) Mean PI + RI > 95% and B notch		30–34 wks	(1) 58.0		(1) 95.8		(1) 53.3		(1) 87.6	
				(2) 63.1		(2) 89.5		(2) 38.7		(2) 95.8	
				(3) 57.5		(3) 98.2		(3) 75.0		(3) 87.3	

UtA uterine artery, *PI* pulsatility index, *RI* resistance index, *U/B notches* unilateral/bilateral notches, *E* early, *DR* detection rate, *FPR* false positive rate, *S* severe, *Primi* primigravida, *PE* pre-eclampsia, *FGR* fetal growth restriction, *SGA* small for gestation age, *LRP* low risk pregnancy, *wks* weeks

The need for today is a combination of test that can perform better in association with UtA Doppler to maintain high sensitivity and specificity in prediction of PE and FGR. Furthermore, because the pathogenesis of preeclampsia has not been fully elucidated, the search for predictive markers and an absolute preventive strategy shall remain an unfulfilled goal [101–103]. The quest for newer markers either alone or in combination to improve the specificity of prevailing tests do exist. However, it is time now to implement these tests in routine practice with the current evidence available.

Conclusion

With the current standards of prenatal care, we have not yet devised an effective method to screen for relatively common obstetric problem like PE in low-risk population and we are still uncertain about the best screening and monitoring strategies. No single parameter or multiparametric testing is currently 100% sensitive for prediction of PE and FGR. As per the systematic review of WHO in 2004, it had been stated that there is no clinically useful screening test to predict the development of preeclampsia, though advances in the methodology of screening had evolved since then. However, the mortality and morbidity due to PE and FGR demands the need for screening to raise the standards in providing good maternal and fetal healthcare. The idea of using UtA Doppler ultrasonography alone for risk prediction as a part of routine ultrasound screening is questionable as the sensitivity of this test in low risk population is quite low.

Assessment of UtA Doppler in all three trimesters can help in prediction of PE and FGR, but for prevention the goal is to identify the "at-risk" population in the first trimester. After the evidence from the ASPRE trial, it is ideal to identify and triage high risk women in first trimester itself to attain the maximum benefits of aspirin. Low dose aspirin started early in pregnancy in a truly high risk population will serve as an effective way of handling PE and FGR. To identify the high risk population, the inclusion of maternal characteristics, biophysical and biochemical testing along with uterine artery PI at 11–13 weeks of gestation improves the predictive efficacy in screening for PE and FGR.

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