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Multicenter screening for pre-eclampsia and fetal growth restriction by transvaginal uterine artery Doppler at 23 weeks of gestation

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KEYWORDS: Uterine arteries, Doppler sonography, Transvaginal, Screening, Pre-eclampsia, Fetal growth restriction

ABSTRACT

Objective *To determine the value of transvaginal color Doppler assessment of the uterine arteries at 23 weeks of gestation in predicting the subsequent development of pre-eclampsia and fetal growth restriction.*

Patients and methods *Women with singleton pregnancies attending for routine ultrasound examination at 23 weeks in any one of seven hospitals underwent Doppler assessment of the uterine arteries. The presence of an early diastolic notch in the waveform was noted, and the mean pulsatility index of the two arteries was calculated. Screening characteristics in the prediction of pre-eclampsia and the delivery of a low birth-weight infant were calculated.*

Results *Doppler examination of the uterine arteries was attempted in 8335 consecutive singleton pregnancies, satisfactory waveforms were obtained from both vessels in 8202 (98.4%) cases and complete outcome data were available in 7851 (95.7%) of these. The mean gestational age was 23 (range, 22–24) weeks. The mean uterine artery pulsatility index did not change significantly with gestation (*r = *−0.0078;* P = *0.483); the median value was 1.04 and the 95th centile was 1.63. In 9.3% of cases early diastolic notches in the waveform from both uterine arteries were present and in an additional 11.1% of cases there were notches unilaterally. Pre-eclampsia with fetal growth restriction occurred in 42 (0.5%) cases, pre-eclampsia without fetal growth restriction in 71 (0.9%) and fetal growth restriction without pre-eclampsia in 698 (8.9%). The sensitivity of increased pulsatility index above the 95th centile (1.63) for pre-eclampsia with fetal growth restriction was 69%, for pre-eclampsia without fetal growth restriction was 24%, for fetal growth restriction without pre-eclampsia was 13%, for pre-eclampsia irrespective of fetal growth restriction was 41% and for fetal growth restriction irrespective of pre-eclampsia was 16%. The sensitivity of fetal growth restriction defined by the 5th rather than the 10th centile was higher (19% vs. 16%). The sensitivity for both pre-eclampsia and fetal growth restriction was inversely related to the gestational age at delivery; when delivery occurred before 32 weeks, the sensitivity for all cases of pre-eclampsia with fetal growth restriction, pre-eclampsia without fetal growth restriction and fetal growth restriction without pre-eclampsia increased to 93%, 80% and 56%, respectively. The sensitivity of bilateral notches in predicting pre-eclampsia and/or fetal growth restriction was similar to that of increased pulsatility index but the screen-positive rate with notches (9.3%) was much higher than that with increased pulsatility index (5.1%).*

Conclusions *A one-stage color Doppler screening program at 23 weeks identifies most women who subsequently develop severe pre-eclampsia and/or fetal growth restriction.*

INTRODUCTION

Pre-eclampsia and fetal growth restriction (FGR) are major causes of perinatal mortality and morbidity. Both conditions are thought to be the consequence of impaired trophoblastic invasion of the maternal spiral arteries and the physiological reduction in vascular resistance in the uteroplacental circulation[1–6]. Over the last 25 years a number of Doppler ultrasound studies of the uteroplacental circulation have confirmed the original observation that increased impedance to flow in these vessels is associated with an increased risk for subsequent development of pre-eclampsia and/or FGR[7]. However, in these studies the number of patients examined was relatively small, and the studies varied widely in methodology as well as in definitions and prevalence of both abnormal results and adverse outcomes (Table 1)[8–20].

This multicenter study examines the value of transvaginal uterine artery Doppler velocimetry at 23 weeks of gestation in the prediction of pre-eclampsia and/or FGR in about 8000 singleton pregnancies. This gestational age was selected

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Table 1 Results of previous uterine artery Doppler screening studies for the prediction of pre-eclampsia and fetal growth restriction

Reference	n	*Abnormal result*	*GA (weeks)*	*Doppler*	*Screen +ve (%)*	*Pre-eclampsia*		*Fetal growth restriction*	
						Prev. (%)	*Sens. (%)*	*Prev. (%)*	*Sens. (%)*
One-stage screening									
Newnham *et al.* 1990[8]	501	RI > 95th centile	18	CW	4.8	—	—	9.8	6
Bewley *et al.* 1991[9]	917	Mean RI > 95th centile	16–24	CW	5.6	4.6*	24	—	—
	913	Mean RI > 95th centile	16–24	CW	5.7	—	—	12.9	15
Bower *et al.* 1993[10]	2058	RI > 95th or notches	18–22	CW	16.0	2.5†	75	10.9	37
Valensise *et al.* 1993[11]	272	Mean RI > 0.58	22	Color-PW	9.6	3.3†	89	7.7	67
North *et al.* 1994[12]	446	RI > 0.57	19–24	Color-PW	11.9	3.4†	27	—	—
	457	RI > 0.57	19–24	Color-PW	12.3	—	—	6.6	50
Todros *et al.* 1995[13]	916	S/D ratio > 2.7	19–24	CW or PW	6.4	—	—	4.6	12
Irion *et al.* 1998[14]	1159	Mean RI > 0.57	26	Color-PW	12.8	3.3†	26	11	29
Kurdi *et al.* 1998[15]	946	RI > 0.55 & bilateral notches	19–21	Color-PW	12.4	2.2*	62	—	—
	946	Bilateral notches & RI > 0.55 or unilateral notch & RI > 0.65 or mean RI > 0.7	19–21	Color-PW	22.8	—	—	16.5	45
Albaiges *et al.* 2000[16]	1757	Mean PI > 95th	23	Color-PW	5.1	3.7†	35	8.1	21
Two-stage screening									
Steel *et al.* 1990[17]	1014	RI > 0.58	18 & 24	CW & CW	11.6	1.9†	63	9.6	33
Bower *et al.* 1993[18]	2026	Bilateral notches	20 & 24	CW & color-PW	6.1	1.8†	78	—	—
Harrington *et al.* 1996[19]	1204	RI > 95th or notches	20 & 24	CW & color-PW	9.1	3.7‡	77	10.9	32
Frusca *et al.* 1997[20]	419	Mean RI > 0.58	20 & 24	CW & color-PW	8.6	1.9†	50	7.2	43

GA, gestational age; Prev., prevalence; Sens., sensitivity; RI, resistance index; S/D, systolic to diastolic ratio; PI, pulsatility index. *Blood pressure ≥ 140/90 mmHg and proteinuria (> 150 mg/24 h). †Blood pressure ≥ 140/90 mmHg and proteinuria (≥ 300 mg/24 h). ‡Blood pressure rise (systolic ≥ 30 mmHg and diastolic ≥ 25 mmHg) with proteinuria (≥ 500 mg/24 h). CW, continuous wave Doppler without visualizing the vessel; PW, pulsed wave Doppler after indentification of the vessel by B-mode; color-PW, color flow mapping to image the vessel followed by pulsed wave Doppler.

because it is associated with lower false-positive rates than is earlier screening[21,22].

MATERIALS AND METHODS

This multicenter screening study involved Doppler ultrasound examination of the uterine arteries at 22–24 weeks of gestation in women with singleton pregnancies attending for routine antenatal care.

The study was approved by the South Thames Multi Centre research ethics committee, as well as the local ethics committees of individual hospitals. Written informed consent was obtained from all women. Sonographers performing the Doppler studies had received the Certificate of Competence in Doppler of The Fetal Medicine Foundation (http://www.fetalmedicine.com). Quality control of screening, handling of data and verification of adherence to protocols at the different centers was performed on a regular basis by the trial coordinators.

The participating hospitals were Basildon Hospital, Basildon, Greenwich Hospital, London, Harold Wood Hospital, Essex, King George Hospital, Essex, King's College Hospital, London, Queen Mary's Hospital, Sidcup, and University Hospital, Lewisham. The study period was October 1999 to September 2000, but not all hospitals commenced the study at the same time. In these centers, all women attending for routine antenatal care are offered two ultrasound scans during pregnancy. The first is carried out at 11–14 weeks of gestation and the aims are to determine gestational age, diagnose major fetal defects, measure nuchal translucency thickness as part of the screening for chromosomal abnormalities, and determine chorionicity in multiple pregnancies. The second examination is at 22–24 weeks and includes a transabdominal scan for measurement of fetal growth and examination for fetal abnormalities. All women with no major fetal abnormality are offered the option of a transvaginal scan to measure both cervical length, as a method of screening for preterm delivery, and uterine artery Doppler studies to screen for pre-eclampsia and FGR.

The ultrasound machines used for the study were as follows: Acuson SP-10 (Acuson, Mountain View, CA, USA); Aloka 5000 and Aloka 1700 (Aloka, Tokyo, Japan); ATL HDI 3000 and ATL HDI 3500 (ATL, Bothell, WA, USA); Hitachi E2U-MT 20-S1 and Hitachi EUB-525 (Hitachi Europe Ltd., Maidenhead, UK); Toshiba Corevision SSA-350 A, Toshiba Ecocee and Toshiba SSH-140 (Toshiba, Tokyo, Japan); Siemens Sonoline Versa Pro (Siemens, Erlangen, Germany). For the transvaginal scan, women were asked to empty their bladders and were placed in the dorsal lithotomy position. The ultrasound probe was then inserted into the vagina and placed in the anterior fornix for measurement of cervical length as previously described[23]. Subsequently, the probe was moved into the lateral fornix and the uterine artery was identified using color Doppler at the level of the internal cervical os (Figure 1). Pulsed wave Doppler was then used to obtain three similar consecutive waveforms. The pulsatility index (PI) was measured, and the presence or absence of an early diastolic notch was noted. The same was then repeated for the contralateral uterine artery and the mean PI of the two vessels was calculated.

Figure 1 Uterine artery visualized by transvaginal color flow mapping.

Women with a mean PI > 1.6, which in an earlier pilot study represented the 95th centile, were followed up with growth scans, blood pressure measurements and urinalysis for protein at 28, 32 and 36 weeks. Women with normal uterine artery Doppler received routine antenatal care.

Outcome measurements were pre-eclampsia and/or FGR. Pre-eclampsia was defined according to the guidelines of the International Society for the Study of Hypertension in Pregnancy. This requires two recordings of diastolic blood pressure of ≥ 90 mmHg at least 4 h apart in previously normotensive women, and proteinuria of 300 mg or more in 24 h, or two readings of at least + + on dipstick analysis of midstream or catheter urine specimens if no 24-h collection is available[24]. Fetal growth restriction was defined as a birth weight < 10th centile for gestation[25].

Demographic characteristics and Doppler findings were recorded in a computer database at the time of the Doppler studies in each participating center. Data on pregnancy outcome were obtained from examination of individual patient notes and labor ward records.

For comparison of results with previous studies, a literature search was carried out that identified 13 uterine artery Doppler studies in unselected populations that provided sufficient data to allow calculation of the performance of the test (Table 1)[8–20].

Statistical analysis

The chi square test or Fisher's exact test were used to analyze categoric variables, and the unpaired *t*-test, Mann–Whitney *U*-test and linear regression were used for continuous variables' analysis where appropriate. Two-sided significance tests are reported. The sensitivity, false positive rate, positive predictive value, negative predictive value and likelihood ratio with 95% confidence intervals for a cut-off mean PI of 1.63 (the 95th centile) and presence of notch bilaterally in the prediction of pre-eclampsia and/or FGR were calculated, and receiver operating characteristic curves were constructed. Statistical analysis was performed using MS Excel 2000 and Arcus Quickstat Biomedical, Version 1.2.

Table 2 Differences between women included in the study and those lost to follow-up

Characteristic	*Included in study* (n = *7851*)	*Lost to follow-up* (n = *351*)	P
Age (years, mean (range))	29.7 (16–47)	29.4 (17–46)	0.3
Body mass index (mean (range))	25.5 (11–74)	25.2 (14–44)	0.6
UtA pulsatility index (mean (range))	1.09 (0.40–3.83)	1.07 (0.49–2.04)	0.6
White (*n* (%))	5859 (74.6)	236 (67.2)	0.003
Black (*n* (%))	1200 (15.3)	86 (24.5)	< 0.001
Asian (*n* (%))	598 (7.6)	24 (6.8)	0.6
Oriental (*n* (%))	95 (1.2)	4 (1.1)	1
Other (*n* (%))	99 (1.3)	1 (0.3)	0.1
Nulliparous (*n* (%))	2821 (35.9)	142 (40.5)	0.09
Cigarette smoker (*n* (%))	1391 (17.7)	41 (11.7)	0.003
UtA pulsatility index > 95th centile (*n* (%))	401 (5.1)	14 (4.0)	0.4
Bilateral UtA notches (*n* (%))	728 (9.3)	29 (8.3)	0.2

UtA, uterine artery.

RESULTS

Doppler examination of the uterine arteries was attempted in 8335 consecutive singleton pregnancies, satisfactory waveforms were obtained from both vessels in 8202 (98.4%) cases and complete outcome data were available in 7851 (95.7%) of these. The mean gestational age was 23 (range, 22–24) weeks. The demographic and screening characteristics of the 7851 pregnancies with follow-up (study population), and those lost to follow-up are compared in Table 2. The only significant difference between the groups was that in those lost to follow-up there was a higher percentage of black women and a lower percentage of cigarette smokers.

In the study population the mean uterine artery PI did not change significantly with gestation ($r = -0.0078$; $P = 0.483$), the median value was 1.04 and the 95th centile was 1.63 (Figure 2). In 9.3% of cases early diastolic notches in the waveform from both uterine arteries were present and in an additional 11.1% of cases there were notches unilaterally (Table 3). Pre-eclampsia with FGR occurred in 42 (0.5%) cases, pre-eclampsia without FGR in 71 (0.9%) and FGR without pre-eclampsia in 698 (8.9%).

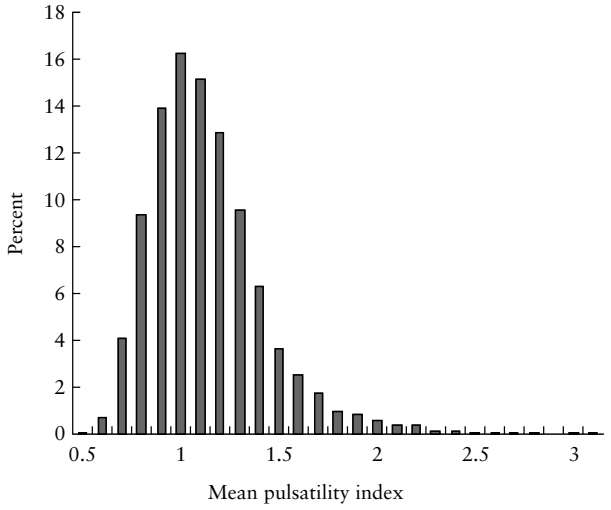

Figure 2 Frequency distribution of the mean pulsatility index in the study population.

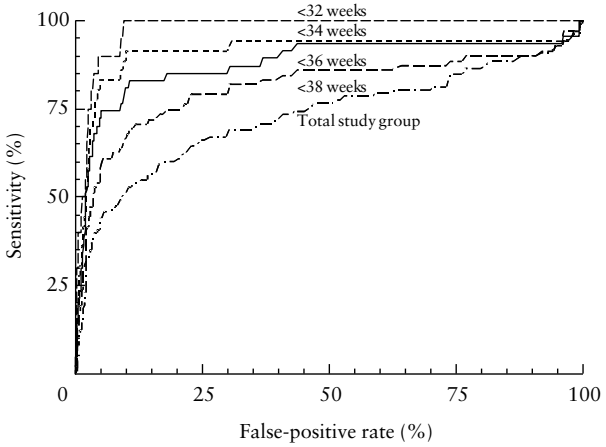

Figure 3 Receiver operating characteristic curve showing that the sensitivity of the uterine artery mean pulsatility index in the prediction of pre-eclampsia, for a given false-positive rate, increases with the severity of the disease as defined by earlier gestational age at delivery.

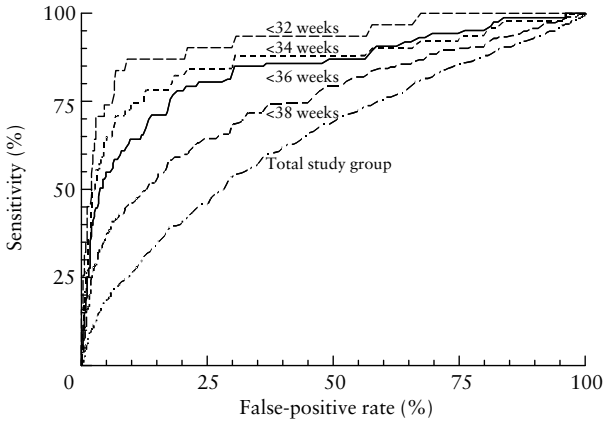

Figure 4 Receiver operating characteristic curve showing that the sensitivity of the uterine artery mean pulsatility index in the prediction of fetal growth restriction, for a given false-positive rate, increases with the severity of the disease as defined by earlier gestational age at delivery.

Table 3 Results of uterine artery Doppler screening in the study population (n = 7851)

Screening index	n	%
Mean pulsatility index > 95th centile (1.63)	401	5.1
Mean pulsatility index > 1.63 and bilateral notches	197	2.5
Mean pulsatility index > 1.63 or bilateral notches	932	11.9
Bilateral notches	728	9.3
Unilateral notches	875	11.1

Screening characteristics for pre-eclampsia and FGR (both for the total group and in subgroups according to gestational age at delivery) are shown in Tables 4–6; in Table 4 for a mean PI > 95th centile, irrespective of the presence or absence of uterine artery notches, in Table 5 for bilateral notches irrespective of mean PI, and in Table 6 for a mean PI > 95th centile or bilateral notches. The essential findings are that increased PI is better at predicting pre-eclampsia with FGR (sensitivity 69%) than pre-eclampsia (23.9%) or FGR (13.2%) alone, and that the sensitivity increases with the severity of the disease as defined by earlier gestational age at delivery

Table 4 Screening characteristics for mean pulsatility index > 1.63, which was found in 401 of the 7851 (5.1%) pregnancies

Characteristic	n	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*LR*	*95% CI*
Total study group							
Pre-eclampsia and FGR	42	69.0	95.2	7.2	99.8	14.5	11.1–17.6
Pre-eclampsia no FGR	71	23.9	95.1	4.2	99.3	4.9	3.1–7.2
FGR no pre-eclampsia	698	13.2	95.7	22.9	91.8	3.1	2.4–3.8
Delivery before 38 weeks							
Pre-eclampsia and FGR	38	71.1	95.2	6.7	99.9	14.8	11.4–18.0
Pre-eclampsia no FGR	34	35.3	95.0	3.0	99.7	7.1	4.3–10.6
FGR no pre-eclampsia	151	25.8	95.3	9.7	95.3	5.5	4.1–7.2
Delivery before 36 weeks							
Pre-eclampsia and FGR	31	77.4	95.2	6.0	99.9	16.1	12.3–19.1
Pre-eclampsia no FGR	16	56.3	95.0	2.2	99.9	11.2	6.6–15.7
FGR no pre-eclampsia	56	39.3	95.1	5.5	99.5	8.1	5.6–11.0
Delivery before 34 weeks							
Pre-eclampsia and FGR	25	84.0	95.1	5.2	99.9	17.3	13.3–20.2
Pre-eclampsia no FGR	11	72.7	95.0	2.0	100	14.5	8.6–18.6
FGR no pre-eclampsia	27	44.4	95.0	3.0	99.8	8.9	5.5–12.8
Delivery before 32 weeks							
Pre-eclampsia and FGR	15	93.3	95.1	3.5	100	18.9	14.1–21.4
Pre-eclampsia no FGR	5	80.0	94.9	1.0	100	15.8	7.4–19.8
FGR no pre-eclampsia	16	56.3	95.0	2.3	99.9	11.2	6.6–15.7

PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; CI, confidence interval; FGR, fetal growth restriction.

Table 5 Screening characteristics for presence of bilateral notches, which was found in 728 of the 7851 (9.3%) pregnancies

Characteristic	n	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*LR*	*95% CI*
Total study group							
Pre-eclampsia and FGR	42	64.3	91.0	3.7	99.8	7.2	5.4–8.7
Pre-eclampsia no FGR	71	25.4	90.9	2.5	99.3	2.8	1.8–4.0
FGR no pre-eclampsia	698	19.9	91.8	19.1	92.2	2.4	2.0–2.9
Delivery before 38 weeks							
Pre-eclampsia and FGR	38	71.1	91.0	3.7	99.8	7.9	6.1–9.4
Pre-eclampsia no FGR	34	35.3	90.8	1.6	99.7	3.9	2.3–5.7
FGR no pre-eclampsia	151	29.8	91.1	6.2	98.5	3.4	2.6–4.3
Delivery before 36 weeks							
Pre-eclampsia and FGR	31	71.0	91.0	3.0	99.9	7.9	5.9–9.5
Pre-eclampsia no FGR	16	50.0	90.8	1.1	99.9	5.4	3.0–7.9
FGR no pre-eclampsia	56	37.5	90.9	2.9	99.5	4.1	2.8–5.6
Delivery before 34 weeks							
Pre-eclampsia and FGR	25	76.0	90.9	2.6	99.9	8.4	6.2–10.0
Pre-eclampsia no FGR	11	45.5	90.8	0.7	99.9	4.9	2.3–7.9
FGR no pre-eclampsia	27	48.1	90.9	1.8	99.8	5.3	3.3–7.3
Delivery before 32 weeks							
Pre-eclampsia and FGR	15	86.7	90.9	1.8	100	9.5	6.8–10.9
Pre-eclampsia no FGR	5	60.0	90.8	0.4	100	6.5	2.5–9.7
FGR no pre-eclampsia	16	62.5	90.8	1.4	99.9	6.8	4.2–9.0

PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; CI, confidence interval; FGR, fetal growth restriction.

Table 6 Screening characteristics for mean pulsatility index > 1.63 or presence of bilateral notches, which was found in 932 of the 7851 (11.9%) pregnancies

Characteristic	n	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*LR*	*95% CI*
Total study group							
Pre-eclampsia and FGR	42	83.3	88.5	3.8	99.9	7.3	6.0–8.2
Pre-eclampsia no FGR	71	40.8	88.4	3.1	99.4	3.5	2.6–4.6
FGR no pre-eclampsia	698	24.4	89.3	18.2	92.4	2.3	2.0–2.6
Delivery before 38 weeks							
Pre-eclampsia and FGR	38	86.8	88.5	3.5	99.9	7.5	6.3–8.4
Pre-eclampsia no FGR	34	58.8	88.3	2.1	99.8	5.0	3.6–6.4
FGR no pre-eclampsia	151	35.8	88.6	5.8	98.6	3.1	2.5–3.9
Delivery before 36 weeks							
Pre-eclampsia and FGR	31	87.1	88.4	2.9	99.9	7.5	6.1–8.4
Pre-eclampsia no FGR	16	81.3	88.3	1.4	100	6.9	4.8–8.1
FGR no pre-eclampsia	56	44.6	88.4	2.7	99.6	3.8	2.8–5.0
Delivery before 34 weeks							
Pre-eclampsia and FGR	25	92.0	88.4	2.5	100	7.9	6.4–8.7
Pre-eclampsia no FGR	11	81.8	88.2	1.0	100	6.9	4.4–8.2
FGR no pre-eclampsia	27	51.8	88.3	1.5	99.8	4.4	2.9–6.0
Delivery before 32 weeks							
Pre-eclampsia and FGR	15	100	88.3	1.6	100	8.5	6.4–8.9
Pre-eclampsia no FGR	5	100	88.2	0.5	100	8.5	4.1–8.6
FGR no pre-eclampsia	16	68.8	88.2	1.2	99.9	5.8	3.8–7.4

PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; CI, confidence interval; FGR, fetal growth restriction.

Table 7 Likelihood ratios of uterine artery Doppler screening in the prediction of pre-eclampsia

		Positive test		*Negative test*	
Reference	n	*LR*	*95% CI*	*LR*	*95% CI*
Steel *et al.* 1990[17]	1014	5.93	3.73–8.17	0.41	0.21–0.66
Bewley *et al.* 1991[9]	917	5.08	2.69–9.03	0.80	0.64–0.91
Bower *et al.* 1993[10]	2058	5.19	4.17–6.14	0.29	0.18–0.45
Valensise *et al.* 1993[11]	272	12.99	7.16–20.99	0.12	0.02–0.47
North *et al.* 1994[12]	446	2.35	0.93–4.88	0.83	0.54–1.01
Irion *et al.* 1998[14]	1159	2.14	1.19–3.51	0.84	0.66–0.97
Harrington *et al.* 1996[19]	1204	11.79	8.84–15.28	0.24	0.14–0.40
Frusca *et al.* 1997[20]	419	6.42	2.62–11.71	0.54	0.23–0.85
Kurdi *et al.* 1998[15]	946	5.51	3.52–7.59	0.43	0.23–0.67
Albaiges *et al.* 2000[16]	1757	7.63	5.38–10.42	0.59	0.46–0.71
Present study	7851	8.87	6.86–11.17	0.62	0.52–0.71
Pooled LR	18 043	6.61	5.90–7.35	0.55	0.50–0.60

LR, likelihood ratio; CI, confidence interval.

Table 8 Likelihood ratios of uterine artery Doppler screening in the prediction of fetal growth restriction

		Positive test		*Negative test*	
Reference	n	*LR*	*95% CI*	*LR*	*95% CI*
Newnham *et al.* 1990[8]	501	1.32	0.42–3.87	0.98	0.87–1.03
Steel *et al.* 1990[17]	1014	3.52	2.46–4.91	0.74	0.63–0.84
Bower *et al.* 1993[10]	2058	2.79	2.26–3.41	0.72	0.65–0.79
Bewley *et al.* 1991[9]	913	3.57	2.08–6.01	0.89	0.81–0.94
Valensise *et al.* 1993[11]	272	13.94	7.33–25.69	0.35	0.18–0.57
North *et al.* 1994[12]	457	5.21	3.18–7.98	0.55	0.37–0.74
Todros *et al.* 1995[13]	916	1.93	0.81–4.24	0.94	0.80–1.01
Harrington *et al.* 1996[19]	1204	5.06	3.58–7.04	0.73	0.64–0.81
Irion *et al.* 1998[14]	1159	2.68	1.93–3.67	0.80	0.70–0.88
Frusca *et al.* 1997[20]	419	7.33	4.05–12.56	0.60	0.42–0.77
Kurdi *et al.* 1998[15]	946	2.43	1.92–3.03	0.68	0.58–0.77
Albaiges *et al.* 2000[16]	1757	3.76	2.60–5.34	0.83	0.75–0.89
Present study	7851	4.15	3.40–5.06	0.87	0.84–0.90
Pooled LR	19 467	3.67	3.34–4.03	0.80	0.78–0.82

LR, likelihood ratio; CI, confidence interval.

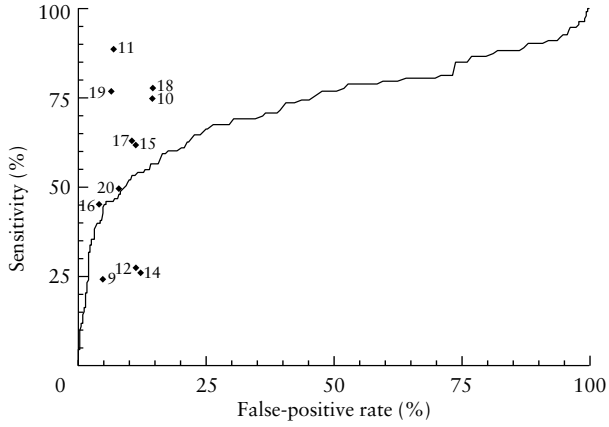

Figure 5 Receiver operating characteristic curve for the prediction of pre-eclampsia in this study. Also shown are the sensitivity and false-positive rate of previous studies (references are indicated).

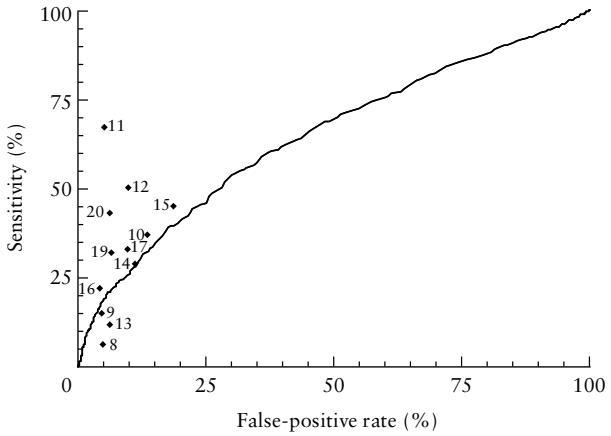

Figure 6 Receiver operating characteristic curve for the prediction of fetal growth restriction in this study. Also shown are the sensitivity and false-positive rate of previous studies (references are indicated).

(Table 4, Figures 3 and 4). The sensitivity of bilateral notches in predicting these complications (Table 5) was similar to that of increased PI but the screen-positive rate with notches (9.3%) was much higher than it was with increased PI (5.1%). The best sensitivities were achieved by defining an abnormal result as either high PI or the presence of notches but the screen-positive rate was increased to 11.9% (Table 6).

The likelihood ratios for pre-eclampsia and FGR in this and the previous screening studies are shown in Tables 7 and 8, respectively. In some of the studies raw data were not provided and numbers for the 2×2 tables were calculated from the reported prevalence, sensitivity and specificity. Two studies reported on the same study population using different methodology (one-stage vs. two-stage screening) and only one of these has been included in Tables 7 and 8[10,18].

Figures 5 and 6 compare the sensitivity and false-positive rate in the prediction of pre-eclampsia and FGR, respectively, in the present and previous studies. Table 9 summarizes the sensitivity of Doppler screening for pre-eclampsia and FGR according to severity of the disease in the present and previous studies.

DISCUSSION

This multicenter screening study demonstrates the feasibility of incorporating Doppler assessment of the uterine arteries into the routine second-trimester scan. Using transvaginal

Table 9 Uterine artery Doppler screening studies reporting on the sensitivity of predicting more severe forms of pre-eclampsia or fetal growth restriction

Reference	*Screen +ve (%)*	*Disease*	*Sensitivity (%)*
Albaiges *et al.* 2000[16]	5.1	Pre-eclampsia	35
		Pre-eclampsia delivery < 34 weeks	80
		FGR < 10th centile	21
		FGR < 10th centile delivery < 34 weeks	70
Kurdi *et al.* 1998[15]	12.4	Pre-eclampsia	62
		Pre-eclampsia delivery < 37 weeks	88
	22.8	FGR < 5th centile	47
		FGR < 5th centile delivery < 37 weeks	100
Harrington *et al.* 1996[19]	9.1	Pre-eclampsia	55
		Pre-eclampsia delivery < 35 weeks	81
		FGR < 10th centile	22
		FGR < 10th centile delivery < 35 weeks	58
Bewley *et al.* 1991[9]	5.7	FGR < 10th centile	15
		FGR < 5th centile	19
Bower *et al.* 1993[10]	6.1	FGR < 10th centile	37
		FGR < 5th centile	46
Steel *et al.* 1990[17]	11.6	FGR < 10th centile	33
		FGR < 5th centile	43
Present study	5.1	Pre-eclampsia	41
		Pre-eclampsia delivery < 34 weeks	81
		FGR < 5th centile	19
		FGR < 10th centile	16
		FGR < 10th centile delivery < 34 weeks	64

sonography and color flow mapping it was possible to visualize both uterine arteries and obtain satisfactory waveforms in about 98% of the patients examined. We have previously reported that the uptake of transvaginal sonography at 22–24 weeks among women attending for routine antenatal care is 80% and that more than 90% of these find the procedure to be associated with no or only mild discomfort and embarrassment, whilst 85% find the ultrasound scan to be as uncomfortable as or less uncomfortable than a speculum examination[23].

The distribution of mean PI was skewed to the left and the 95th centile was 1.63. The 5% of the population with a mean PI > 1.63 contained 69% of women destined to develop pre-eclampsia with FGR, 24% of those who developed pre-eclampsia alone and 13% of those who delivered a growth-restricted baby in the absence of pre-eclampsia. The sensitivities for pre-eclampsia irrespective of FGR (41%) and FGR irrespective of pre-eclampsia (16%), for the same-screen positive rate, were broadly similar to those in most previous studies, but lower than in some and higher than in others (Figures 5 and 6).

Our results are similar to those of a previous study[16] in which we also examined the value of one-stage screening at 23 weeks using color flow equipment to visualize the uterine arteries, except that in that study we used transabdominal, rather than transvaginal, Doppler. Both studies have demonstrated that for the same screen-positive rate the sensitivity of mean PI for both pre-eclampsia and delivery of a small-for-gestational age baby is better than that with bilateral notches. Although in the group with bilateral notches and normal PI there were some cases with adverse outcome, inclusion of bilateral notches in the definition of the screen-positive group introduces an element of subjectivity into the program and doubles the screen-positive rate with only a small improvement in sensitivity.

The findings of the study demonstrate that Doppler screening at 23 weeks is much better at identifying the more severe and therefore clinically most relevant cases of pre-eclampsia and FGR. Firstly, the sensitivity for pre-eclampsia with FGR (69%) was nearly three times as high as that for pre-eclampsia without FGR (24%). Secondly, the sensitivity of FGR defined by the 5th rather than the 10th centile was higher (19% compared to 16%). Thirdly, the sensitivity for both pre-eclampsia and FGR was inversely related to the gestational age at delivery; the sensitivity for all cases of pre-eclampsia with FGR (69%), pre-eclampsia without FGR (24%) and FGR without pre-eclampsia (13%) increased to 93%, 80% and 56%, respectively, for these complications requiring delivery before 32 weeks.

In this study screening was performed in several maternity ultrasound departments providing routine antenatal care, rather than in specialized clinics by highly trained and motivated researchers as in previous studies. This pragmatic approach to screening has shown that the great majority of women destined to develop the serious complications of impaired placentation can be identified. Accurate prediction of those women destined to develop severe pre-eclampsia and/or FGR followed by increased surveillance and timely intervention may improve outcome. Implementation of a uterine artery screening program into routine antenatal care would help stratify the intensity of subsequent surveillance because in those with increased mean PI there is a six-fold increase in likelihood of serious complications whereas in those with a normal PI there is a halving of such likelihood.

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APPENDIX

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