

Prediction of pre-eclampsia by a combination of maternal history, uterine artery Doppler and mean arterial pressure

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KEYWORDS: blood pressure; Doppler; pre-eclampsia; screening

ABSTRACT

Objectives To determine the value of combined screening for pre-eclampsia by maternal history, and mid-trimester uterine artery (UtA) Doppler imaging and maternal blood pressure.

Methods In 3529 singleton pregnancies attending for routine care at 22–24 weeks' gestation we recorded maternal variables, and made UtA Doppler and mean arterial pressure (MAP) measurements. Multiple regression analysis was used to determine the significant predictors of pre-eclampsia, gestational hypertension and small-for-gestational age (SGA) among maternal characteristics, UtA pulsatility index (PI) and MAP.

Results Complete pregnancy outcomes were available in 3359/3529 (95.2%) cases. Pre-eclampsia developed in 101 (3.0%) pregnancies, including 23 (0.7%) in which delivery was before 34 weeks (early pre-eclampsia) and 78 (2.3%) with delivery at 34 weeks or more (late pre-eclampsia); 74 (2.2%) developed gestational hypertension, 366 (10.9%) delivered SGA newborns with no hypertensive disorders, and 2806 (83.8%) were unaffected by pre-eclampsia, gestational hypertension or SGA. Multiple regression analysis demonstrated that maternal characteristics, UtA-PI and MAP provided a significant independent contribution in the prediction of pre-eclampsia, gestational hypertension and SGA. For a false-positive rate of 10%, the estimated detection rates of early and late pre-eclampsia were 100% and 56.4%, respectively.

Conclusions The combination of maternal demographic characteristics, and UtA Doppler and maternal blood pressure measurements is an effective screening tool for the prediction of pre-eclampsia. Copyright © 2008 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Pre-eclampsia, which affects about 2% of pregnancies, is thought to be the consequence of impaired trophoblastic invasion of the maternal spiral arteries and their conversion from narrow vessels to wide non-muscular channels. However, in women with pre-eclampsia the prevalence of placental lesions is inversely related to the gestational age at delivery^{1,2}. It is early disease, requiring delivery before 34 weeks and found in 0.5% of pregnancies, which is associated with fetal growth restriction and increased risk of perinatal mortality and morbidity, and both short-term and long-term maternal complications^{3–5}.

In this screening study we investigated the potential value of combining a number of factors in the maternal history, including ethnic origin, parity, body mass index (BMI) and personal or family history of pre-eclampsia^{4,5}, with uterine artery (UtA) pulsatility index (PI) and mean arterial pressure (MAP) in the prediction of early and late pre-eclampsia.

METHODS

This was a prospective screening study for pre-eclampsia in singleton pregnancies attending for routine antenatal care. The study was approved by King's College Hospital Ethics Committee.

In our hospital all women are offered one ultrasound examination at 11 + 0 to 13 + 6 weeks, for pregnancy dating and early diagnosis of major chromosomal and other fetal abnormalities, and another assessment at 22 + 0 to 24 + 6 weeks, which includes transabdominal sonography for examination of the fetal anatomy and growth, and transvaginal sonography for measurement of cervical length and measurement of UtA-PI. Gestational age is determined from the menstrual history and

confirmed from the measurement of fetal crown–rump length at the first-trimester scan.

Patients were asked to complete a questionnaire on maternal age, ethnic origin (Caucasian, Afro-Caribbean, Indian or Pakistani, Chinese or Japanese, and mixed), cigarette smoking during pregnancy (yes or no), medical history (including chronic hypertension, diabetes mellitus, antiphospholipid syndrome, thrombophilia, human immunodeficiency virus infection and sickle cell disease), methods of conception (spontaneous, use of ovulation drugs or *in-vitro* fertilization (IVF)), parity (parous or nulliparous if no delivery beyond 23 weeks), obstetric history (including previous pregnancy with pre-eclampsia) and family history of pre-eclampsia. Maternal weight and height were measured, and BMI was calculated.

Blood pressure was taken by validated automated devices (3BTO-A2, Microlife, Taipei, Taiwan), which were calibrated before and at regular intervals during the study⁶. The recordings were made by doctors who had received appropriate training on the use of these machines. The women were in the seated position, their arms were supported at the level of the heart, and either a small (< 22 cm), normal (22–32 cm) or large (33–42 cm) adult cuff was used depending on the mid-arm circumference⁷. After resting for 5 min blood pressure was measured in both arms simultaneously, and a series of recordings were made at 1-min intervals until variations between consecutive readings fell within 10 mmHg in systolic pressure and 6 mmHg in diastolic pressure (DBP) in both arms⁸. When this point of stability was reached we calculated the MAP of each arm as the average of the last two stable measurements and, as recommended, we took the arm with the highest final MAP for the subsequent analysis of results⁸.

Doppler examinations were performed by experienced sonographers who had obtained the appropriate certificates of competence of The Fetal Medicine Foundation (<http://www.fetalmedicine.com>). Color flow mapping was used to identify in turn the left and right UtAs, and pulsed-wave Doppler imaging was used to measure the PI⁹. The mean PI of the two vessels was calculated⁹.

The MAP, ultrasound findings and characteristics of the women, including demographic data and obstetric and medical history, were entered into a computer database. Data on pregnancy outcome were collected from the hospital maternity records or their general medical practitioners. The obstetric records of all women with pre-existing or pregnancy-associated hypertension were examined by assessors who were not aware of the screening results to determine whether the condition was chronic hypertension, pre-eclampsia or gestational hypertension.

Outcome measures

The outcome measures were pre-eclampsia, gestational hypertension and small-for-gestational age (SGA). In pre-eclampsia and gestational hypertension we included all

cases with SGA, but in SGA we excluded cases with pre-eclampsia or gestational hypertension. The pre-eclampsia group included those with pre-eclampsia superimposed on chronic hypertension.

The definitions of pre-eclampsia and gestational hypertension were those of the International Society for the Study of Hypertension in Pregnancy¹⁰. In gestational hypertension the DBP should be 90 mmHg or more on at least two occasions 4 h apart, developing after 20 weeks of gestation in previously normotensive women in the absence of significant proteinuria. In pre-eclampsia there should be gestational hypertension with 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. In chronic hypertension there should be a history of hypertension before conception or the presence of hypertension at the booking visit before 20 weeks of gestation in the absence of trophoblastic disease. In pre-eclampsia superimposed on chronic hypertension significant proteinuria (as defined above) should develop after 20 weeks of gestation in women with known chronic hypertension¹⁰.

In all women the birth weight was converted into a percentile after correction for gestational age at delivery, sex of the newborn, maternal ethnic origin, weight, height and parity¹¹. The newborn was considered to be SGA if the birth weight was less than the 10th percentile.

Statistical analysis

The following six steps were taken. First, the women were subdivided into five groups depending on pregnancy outcome: early pre-eclampsia; late pre-eclampsia; gestational hypertension; SGA; and unaffected by pre-eclampsia, gestational hypertension or SGA. Second, the distributions of UtA-PI and MAP were made Gaussian after logarithmic transformation. Third, multiple regression analysis was used to determine which of the factors among the maternal characteristics, medical and obstetric history, and gestation were significant predictors of log UtA-PI and log MAP in the unaffected group. Fourth, the distributions of log UtA-PI and log MAP, expressed as multiples of the median (MoM) of the unaffected group, were determined in the pre-eclampsia, gestational hypertension and SGA groups. Fifth, multiple regression analysis was used to determine factors, including log MoM UtA-PI and log MoM MAP, that had a significant contribution in predicting early pre-eclampsia, late pre-eclampsia, gestational hypertension and SGA. Sixth, the detection and false-positive rates were calculated as the respective proportions of pre-eclampsia, gestational hypertension and SGA (detection rate) and unaffected pregnancies (false-positive rate) with MoM values above given cut-offs.

The statistical software package SPSS version 12.0 (SPSS Inc., Chicago, IL, USA) was used for all data analyses.

RESULTS

Patient characteristics

Second-trimester screening was carried out in 3529 consecutive singleton pregnancies attending our hospital at 22–24 weeks of gestation from July 2006, and included all women with expected delivery up to October 2007. We excluded 182 (5.2%) because they had missing outcome data ($n = 170$), the pregnancies resulted in fetal death or miscarriage before 24 weeks of gestation ($n = 10$), or the pregnancies were terminated owing to fetal abnormalities ($n = 2$). The median maternal age was lower, there were more women of Indian or Pakistani origin, fewer Caucasian women and more women with no previous history of pre-eclampsia among the excluded cases compared with those included in the analysis (Table 1).

Among the remaining 3347 women, 101 (3.0%) developed pre-eclampsia, including 23 (0.7%) in whom

delivery was before 34 weeks (early pre-eclampsia) and 78 (2.3%) with delivery at 34 weeks or more (late pre-eclampsia), 74 (2.2%) who developed gestational hypertension, 366 (10.9%) who delivered SGA newborns but did not develop pre-eclampsia or gestational hypertension, and 2806 (83.8%) who were unaffected by pre-eclampsia, gestational hypertension or SGA. The characteristics of the five outcome groups are summarized in Table 1.

Uterine artery pulsatility index and mean arterial pressure

In the multiple regression model for log UtA-PI significant independent contributions were provided by maternal ethnic origin and cigarette smoking; for log MAP significant independent contributions were provided by maternal ethnic origin, BMI, previous history of pre-eclampsia and method of conception. The multiple regression equations were:

Table 1 Maternal characteristics, and medical and obstetric history in the five groups of pregnancy outcome and those excluded from the study

Maternal characteristic	Unaffected ($n = 2806$)	Early pre-eclampsia ($n = 23$)	Late pre-eclampsia ($n = 78$)	Gestational hypertension ($n = 74$)	SGA ($n = 366$)	Excluded ($n = 182$)
Maternal age (years)	31.6 (16–49)	28.6 (17–40)	31.1 (19–49)	33.9 (17–44)†	30.9 (16–44)	30.6 (16–44)†
Body mass index (kg/m^2)	26.3 (16.4–53.9)	29.8 (21.9–40.4)‡	29.9 (21.1–47.4)‡	28.2 (21.9–46.9)‡	26.0 (15.5–50.4)	26.9 (17.3–43.2)
Ethnicity						
Caucasian	1482 (52.8)	4 (17.4)‡	23 (29.5)‡	45 (60.8)	170 (46.4)‡	74 (40.7)†
Afro-Caribbean	1028 (36.6)	17 (73.9)‡	46 (59.0)‡	26 (35.1)	157 (42.9)*	78 (42.9)
Indian or Pakistani	132 (4.7)	0 (0)	4 (5.1)	0 (0)	13 (3.6)	17 (9.3)*
Chinese or Japanese	49 (1.7)	0 (0)	2 (2.6)	0 (0)	4 (1.1)	2 (1.1)
Mixed	115 (4.1)	2 (8.7)	3 (3.8)	3 (4.1)	22 (6.0)	11 (6.0)
Family history of pre-eclampsia	85 (3.0)	3 (13.0)*	9 (11.5)*	8 (10.8)†	11 (3.0)	2 (1.1)
Parity						
Nulliparous	1383 (49.3)	11 (47.8)	47 (60.3)‡	43 (58.1)	199 (54.4)	107 (58.8)
Parous – no previous pre-eclampsia	1367 (48.7)	8 (34.8)	22 (28.2)†	25 (33.8)*	163 (44.5)	70 (38.5)†
Parous – previous pre-eclampsia	56 (2.0)	4 (17.4)*	9 (11.5)‡	6 (8.1)†	4 (1.1)	5 (2.7)
Cigarette smoker	204 (7.3)	1 (4.3)	5 (6.4)	4 (5.4)	56 (15.3)‡	14 (7.7)
Conception						
Spontaneous	2754 (98.1)	23 (100.0)	76 (97.4)	73 (98.6)	356 (97.3)	178 (97.8)
Ovulation drugs	18 (0.6)	0 (0)	1 (1.3)	0 (0)	5 (1.4)	2 (1.1)
In-vitro fertilization	34 (1.2)	0 (0)	1 (1.3)	1 (1.4)	5 (1.4)	2 (1.1)
Medical history						
None	2736 (97.5)	20 (87.0)*	74 (94.9)	73 (98.6)	359 (98.1)	180 (98.9)
Chronic hypertension	39 (1.4)	3 (13.0)†	4 (5.1)*	0 (0)	0 (0)	2 (1.1)
Diabetes mellitus	8 (0.3)	0 (0)	0 (0)	1 (1.4)	0 (0)	0 (0)
Antiphospholipid syndrome	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.3)	0 (0)
Thrombophilia	14 (0.5)	0 (0)	0 (0)	0 (0)	1 (0.3)	0 (0)
Sickle cell disease	3 (0.1)	0 (0)	0 (0)	0 (0)	2 (0.5)	0 (0)
HIV infection	6 (0.2)	0 (0)	0 (0)	0 (0)	3 (0.8)	0 (0)

Values are median (range) or n (%). Data for adverse pregnancy outcome groups were compared with those of unaffected pregnancies. Data for excluded patients were compared with those of the total group with outcomes. Chi-square test was used to compare categorical variables and ANOVA for continuous variables. * $P < 0.05$. † $P < 0.01$. ‡ $P < 0.001$. HIV, human immunodeficiency virus; SGA, small-for-gestational age.

Log UtA-PI = $-0.0014 + (0.0132 \text{ if Afro-Caribbean, } 0 \text{ if other ethnic origin}) + (0.0261 \text{ if smoker, } 0 \text{ if not smoker}); r^2 = 0.008, P < 0.001$

Log MAP = $1.8544 + 0.0025 \times \text{BMI (kg/m}^2) + (-0.0103 \text{ if Chinese or Japanese, } 0 \text{ if other ethnic origin}) + (-0.0089 \text{ if parous without previous pre-eclampsia, } 0 \text{ if parous with previous pre-eclampsia or nulliparous}) + (0.0195 \text{ if use of ovulation drug, } 0 \text{ if spontaneous or IVF conception}); r^2 = 0.111, P < 0.001.$

The mean log UtA-PI was 0 (95% CI, -0.0036 to 0.0037) MoM in the unaffected group, 0.2797 (95% CI, 0.2378 – 0.3215) MoM in the early pre-eclampsia group, 0.0709 (95% CI, 0.0365 – 0.1053) MoM in the late pre-eclampsia group, 0.0336 (95% CI, 0.0083 – 0.0589) MoM in the gestational hypertension group and 0.0432 (95% CI, 0.0314 – 0.0550) MoM in the SGA group (Figure 1). The mean log MoM UtA-PI in the pre-eclampsia ($t = -7.110, P < 0.001$), gestational hypertension ($t = -2.630, P = 0.01$) and SGA ($t = -7.065, P < 0.001$) groups was significantly higher than in the unaffected group.

The mean log MAP was 0 (95% CI, -0.0009 to 0.0016) MoM in the unaffected group, 0.0681 (95% CI, 0.0406 – 0.0956) MoM in the early pre-eclampsia group, 0.0343 (95% CI, 0.0250 – 0.0437) MoM in the late pre-eclampsia group, 0.0395 (95% CI, 0.0311 – 0.0479) in the gestational hypertension group and 0.0052 (95% CI, 0.0017 – 0.0087) MoM in the SGA group (Figure 2). The mean MoM MAP in the pre-eclampsia and gestational hypertension groups was higher than in the unaffected group ($t = -8.231, P < 0.001$ and $t = -8.889,$

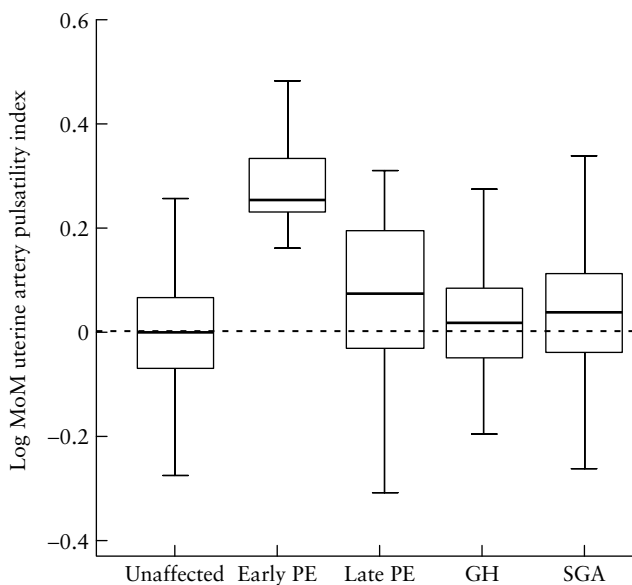


Figure 1 Box-and-whisker plot of log multiples of the median (MoM) uterine artery pulsatility index in unaffected pregnancies, and in those complicated by early and late pre-eclampsia (PE), gestational hypertension (GH) and delivery of small-for-gestational age (SGA) newborns. Median, 25th and 75th centiles, and range are shown.

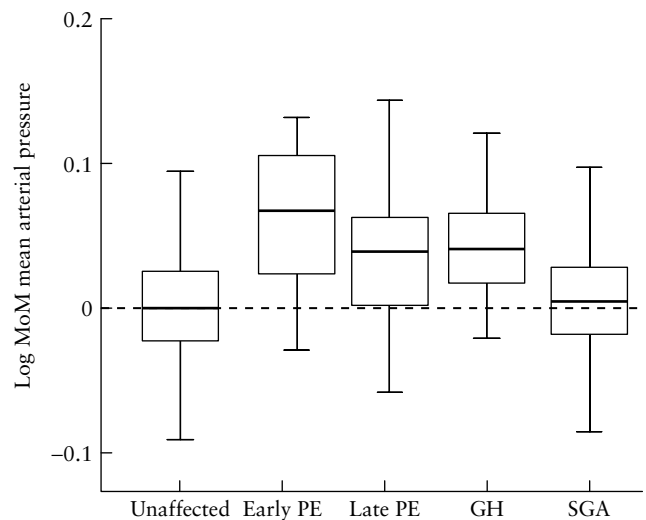


Figure 2 Box-and-whisker plot of log multiples of the median (MoM) mean arterial pressure in unaffected pregnancies, and in those complicated by early and late pre-eclampsia (PE), gestational hypertension (GH) and delivery of small-for-gestational age (SGA) newborns. Median, 25th and 75th centiles, and range are shown.

$P < 0.001$), but was not significantly different in the SGA group ($P = 0.78$)

Patient-specific risks for hypertensive disorders

The patient-specific risk for each outcome (%) was calculated from the formula: $\text{odds}/(1 + \text{odds})$, where $\text{odds} = e^Y$. Y was derived from multiple regression analysis, which demonstrated that the maternal characteristics log MoM UtA-PI and log MoM MAP provided significant independent contribution in the prediction of pre-eclampsia, gestational hypertension and SGA. The multiple regression equations were:

Early pre-eclampsia : $Y = -11.4487 + 31.2443 \times \log \text{ MoM UtA-PI} + 40.1105 \times \log \text{ MoM MAP} + (1.5442 \text{ if Afro-Caribbean, } 0 \text{ if other ethnic groups}); r^2 = 0.747, P < 0.001$

Late pre-eclampsia : $Y = -7.4924 + 6.2361 \times \log \text{ MoM UtA-PI} + 23.1953 \times \log \text{ MoM MAP} + (0.6003 \text{ if Afro-Caribbean, } 0 \text{ if other ethnic groups}) + 0.1197 \times \text{BMI (kg/m}^2) + (-1.1058 \text{ if parous without previous pre-eclampsia, } 0 \text{ if parous with previous pre-eclampsia or nulliparous}); r^2 = 0.236, P < 0.001$

Gestational hypertension : $Y = -8.2383 + 3.5743 \times \log \text{ MoM UtA-PI} + 28.1415 \times \log \text{ MoM MAP} + 0.0477 \times \text{age (years)} + 0.1021 \times \text{BMI (kg/m}^2) + (-0.9810 \text{ if parous without previous pre-eclampsia, } 0 \text{ if parous with previous pre-eclampsia or nulliparous}); r^2 = 0.192, P < 0.001$

SGA : $Y = -2.2473 + 4.4799 \times \log \text{ MoM UtA-PI} + 3.5286 \times \log \text{ MoM MAP} + (0.3145 \text{ if Afro-Caribbean, } 0 \text{ if other ethnic groups}) + (0.9378 \text{ if smoker, } 0 \text{ if not smoker}) + (-0.2333 \text{ if parous without previous pre-eclampsia, } 0 \text{ if parous with previous pre-eclampsia or nulliparous}); r^2 = 0.064, P < 0.001.$

Example of calculation of patient-specific risk for early pre-eclampsia

In a nulliparous black woman who does not smoke, has a BMI of 25 kg/m², conceived spontaneously, and presents with a UtA-PI of 1.6 and MAP of 90 mmHg, the risk for early pre-eclampsia is derived as follows:

Log MoM UtA-PI = 0.2041 - (-0.0014 + 0.0132 for black ethnicity + 0 for non-smoker) = 0.1923

Log MoM MAP = 1.9542 - (1.8544 + 0.0025 × 25 for BMI + 0 for black ethnicity + 0 for nulliparity + 0 for spontaneous conception) = 0.0373

$Y = -11.4487 + 31.2443 \times 0.1923(\log \text{ MoM UtA-PI}) + 40.1105 \times 0.0373 (\log \text{ MoM MAP} + 1.5442 (\text{Afro-Caribbean})) = -2.3978$

Odds = $e^Y = 0.0909$

Risk for early pre-eclampsia = odds/(1 + odds) = 0.0833 (8.334%).

Performance of screening

The estimated detection rates of early and late pre-eclampsia for different false-positive rates in screening by maternal factors only, UtA-PI only, MAP only, and a combination of the three are given in Figures 3 and 4. The performance of the four methods of screening for pre-eclampsia, gestational hypertension and SGA is compared by means of areas under the receiver-operating characteristics curves and detection rates, for a fixed false-positive rate of 10%, in Table 2.

DISCUSSION

In this screening study for hypertensive disorders of pregnancy we examined prospectively a large population

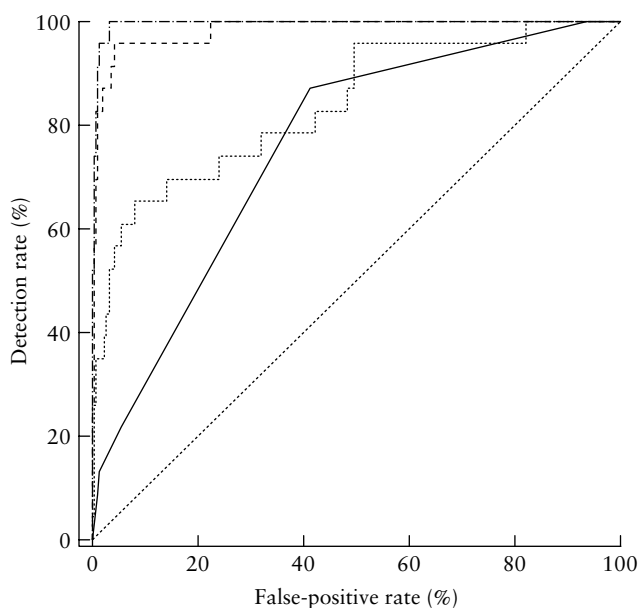


Figure 3 Early pre-eclampsia. Detection and false-positive rates for screening by maternal factors only (—), uterine artery pulsatility index only (- - -), mean arterial pressure only (.....) and a combination of the three (-·-·).

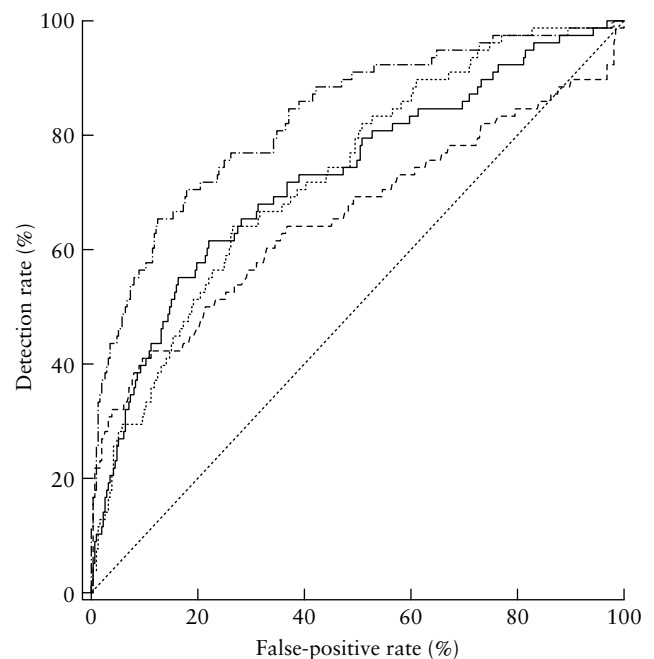


Figure 4 Late pre-eclampsia. Detection and false-positive rates for screening by maternal factors only (—), uterine artery pulsatility index only (- - -), mean arterial pressure only (.....) and a combination of the three (-·-·).

of pregnant women attending for routine care in a well defined gestational age group, and applied a statistical approach that is widely accepted in screening for trisomy 21 to examine the performance of screening and calculate patient-specific risks¹². Appropriately trained doctors recorded basic features from the maternal history, used color Doppler ultrasonography to measure UtA-PI and an automated device to measure blood pressure. We found that combined testing can identify the majority of pregnancies that develop pre-eclampsia and gestational hypertension. The performance of combined screening was substantially better for early than late pre-eclampsia and, for a 10% false-positive rate, the respective detection rates were 100% and 56%.

In the UK, the National Institute for Health and Clinical Excellence has issued guidelines on routine antenatal care, recommending that a woman's level of risk for pre-eclampsia should be evaluated at her first medical visit so that a plan for her schedule of antenatal appointments can be formulated¹³. However, as demonstrated in our study, screening on the basis of maternal characteristics alone would identify only about 30% of pregnancies destined to develop pre-eclampsia, at a false-positive rate of 10%. A more effective approach is one that combines maternal history with measurement of blood pressure and UtA-PI. Our findings that with UtA Doppler the detection rates of early and late pre-eclampsia, at a false positive rate of 10%, were 95.7% and 41.0%, respectively, are compatible with the results of a previous study in 30 775 pregnancies¹⁴. The UtA-PI at 22–24 weeks of gestation was above the 95th centile in 77% of women who developed pre-eclampsia requiring delivery before 34 weeks, in 36% of those delivering at 34–37 weeks and

Table 2 Comparison of the performance of screening for pre-eclampsia, gestational hypertension and small-for-gestational age (SGA) by maternal factors alone, uterine artery pulsatility index (UtA-PI) alone, mean arterial pressure alone and by a combination of the three

Performance of screening test	Pre-eclampsia		Gestational hypertension	SGA
	Early	Late		
Area under ROC curve (mean (95% CI))				
Maternal factors alone	0.752 (0.736–0.768)	0.719 (0.703–0.736)	0.685 (0.668–0.702)	0.586 (0.569–0.603)
UtA-PI	0.983 (0.978–0.988)‡	0.655 (0.637–0.672)	0.572 (0.554–0.590)*	0.609 (0.591–0.626)
Mean arterial pressure	0.840 (0.826–0.853)	0.730 (0.714–0.746)	0.777 (0.761–0.792)*	0.535 (0.517–0.552)*
Combined screening	0.996 (0.993–0.998)‡	0.830 (0.816–0.844)‡	0.836 (0.822–0.849)‡	0.647 (0.630–0.663)‡
Detection rate for 10% FPR (% (95% CI))				
Maternal factors	30.0 (10.0–55.0)	34.6 (24.2–46.2)	23.0 (14.0–34.2)	18.0 (11.8–21.5)
UtA-PI	95.7 (78.0–99.3)	41.0 (30.0–52.7)	20.3 (11.8–31.2)	22.3 (18.1–26.9)
Mean arterial pressure	65.2 (42.7–83.6)	39.7 (28.8–51.5)	39.2 (28.0–51.2)	11.5 (7.7–14.4)
Combined screening	100.0 (85.0–100.0)	56.4 (40.9–64.0)	54.1 (42.1–65.7)	27.3 (21.4–30.6)

Area under receiver–operating characteristics (ROC) curve for each screening method is compared with that for screening by maternal factors alone. * $P < 0.05$, ‡ $P < 0.001$. FPR, false-positive rate.

in 22% of those delivering after 37 weeks. The underlying mechanism for pre-eclampsia is thought to be impaired trophoblastic invasion of the maternal spiral arteries and their conversion from narrow muscular vessels to wide non-muscular channels. The Doppler findings are compatible with data from histological studies^{1,2}, and suggest that there is a wide spectrum of such impaired placentation, with severe impairment leading to early-onset pre-eclampsia and less severe impairment causing late-onset disease¹⁴.

Measurement of blood pressure constitutes the cornerstone of prenatal care. However, in the past 45 years only 10 second-trimester studies have investigated in a combined total of 19 236 women the use of blood pressure measurement as a screening method for subsequent development of pre-eclampsia. These studies have reported contradictory results, with false-positive rates ranging from 7% to 52% and detection rates ranging from 8% to 93%^{15–24}. These differences are likely to be the consequence of the various methods used to select the screened population and measure blood pressure, different cut-offs used in defining the screen-positive group and different definitions of pre-eclampsia. In our study, which used a validated automated device to measure blood pressure and strict criteria to define MAP and pre-eclampsia, the detection rates of early and late pre-eclampsia, for a false-positive rate of 10%, were 65% and 40%, respectively.

We chose 22–24 weeks for screening because at this time in gestation women attend the hospital routinely for an ultrasound examination to identify fetal defects and assess fetal growth and well-being. At the same visit, in addition to examining the fetus, it would be easy to measure the UtA-PI and MAP, and calculate the patient-specific risk for subsequent development of pre-eclampsia. At present there are no prophylactic interventions that can substantially reduce the risk of developing pre-eclampsia^{25–28}. However, the rationale behind the recommended policy of basing the frequency of antenatal visits on the patient-specific risks for pre-eclampsia is that increased surveillance and timely

intervention in women at high risk could potentially improve both maternal and fetal outcome¹⁴. We have demonstrated that, if such assessment of risk is based on a combination of maternal history and measurement of blood pressure and UtA-PI, the detection rate of pre-eclampsia is substantially higher than if screening is based on maternal history alone.

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