Ultrasound Obstet Gynecol 2022; **59**: 335–341
Published online 2 February 2022 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.24829

Estimated fetal weight at mid-gestation in prediction of pre-eclampsia in singleton pregnancy

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KEYWORDS: estimated fetal weight; fetal biometry; impaired placentation; mean arterial pressure; pre-eclampsia; uterine artery Doppler

CONTRIBUTION

What are the novel findings of this work?
Sonographic estimated fetal weight (EFW) at mid-gestation can improve the prediction of early and preterm pre-eclampsia (PE) provided by maternal risk factors and mean arterial pressure (MAP) but not the prediction provided by a combination of maternal risk factors, MAP and uterine artery pulsatility index.

What are the clinical implications of this work?
In pregnancies complicated by preterm PE, a high proportion of babies are small-for-gestational age and EFW measured at the routine mid-gestation ultrasound examination can be used for prediction of preterm PE.

ABSTRACT

Objective *To examine the distribution of birth weight according to gestational age in pregnancies complicated by pre-eclampsia (PE) and assess the potential value of sonographic estimated fetal weight (EFW) at mid-gestation as a predictor of PE.*

Methods *The data for this study were derived from prospective screening for adverse obstetric outcome in 93 911 women with a singleton pregnancy attending for routine pregnancy care at 19 + 0 to 24 + 6 weeks' gestation in two UK maternity hospitals. This visit included recording of maternal demographic characteristics and medical history, sonographic EFW and measurement of mean arterial pressure (MAP) and uterine artery pulsatility index (UtA-PI). The distribution of birth weight of pregnancies with and those without PE was assessed. The competing-risks model was used to estimate the individual, patient-specific risk of delivery with PE at < 32 and < 37 weeks' gestation and at any gestational age. The areas under the receiver-operating-characteristics curves and detection rates (DRs) of delivery with PE, at a 10% false-positive rate (FPR), were assessed for various combinations of maternal risk factors, EFW, MAP and UtA-PI. McNemar's test was used to determine the significance of difference in DR at a 10% FPR between screening with* vs *without EFW.*

Results *The study population contained 2843 (3.0%) pregnancies that subsequently developed PE, including 148 (0.2%) that delivered with PE at < 32 weeks' gestation and 654 (0.7%) that delivered with PE at < 37 weeks. Birth weight was < 10th percentile in 82% of pregnancies with PE delivering at < 32 weeks' gestation and this decreased to 21% of those with PE delivering at ≥ 37 weeks. In screening for delivery with PE at < 32 and < 37 weeks' gestation, the DR, at a 10% FPR, achieved by maternal risk factors (51% and 46%, respectively) was improved by addition of EFW (69% and 51%, respectively). Similarly, addition of EFW improved the performance of screening by a combination of maternal risk factors and MAP from 72% to 80% for PE < 32 weeks and from 57% to 60% for PE < 37 weeks. EFW did not improve the predictive performance of screening by a combination of maternal risk factors, MAP and UtA-PI.*

Conclusions *In pregnancies complicated by preterm PE, a high proportion of neonates are small-for-gestational age, and sonographic EFW at mid-gestation can improve the prediction of early and preterm PE provided by maternal risk factors and MAP but not the prediction provided by a combination of maternal risk factors, MAP and UtA-PI.* © *2021 International Society of Ultrasound in Obstetrics and Gynecology.*

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Accepted: 29 November 2021

INTRODUCTION

Studies have reported that preterm pre-eclampsia (PE) is associated with low birth weight, whereas, in term PE, birth weight is often normal[1–9]. In a previous multicenter study involving 30 639 singleton pregnancies, including 614 (2%) cases that developed PE, we reported that, in the PE group, there was a significant inverse association between gestational age at delivery and prevalence of small-for-gestational-age (SGA) neonate[9]. At mid-gestation, screening by a combination of maternal risk factors, uterine artery pulsatility index (UtA-PI) and mean arterial pressure (MAP) is associated with high predictive performance for preterm PE but not term PE[10]. There is also good evidence that a model combining maternal risk factors, UtA-PI and estimated fetal weight (EFW) at mid-gestation provides useful prediction of SGA, particularly for preterm compared with term cases and for pregnancies with PE[11].

The objective of this screening study of 93 911 singleton pregnancies was to examine further the association between the incidence of SGA neonate and gestational age at delivery in pregnancies complicated by PE and assess the potential value of sonographic EFW at mid-gestation as a predictor of PE.

METHODS

Study design and participants

The data for this study were derived from prospective screening for adverse obstetric outcome in women attending for routine pregnancy care at 19 + 0 to 24 + 6 weeks' gestation at King's College Hospital, London and Medway Maritime Hospital, Gillingham, UK, between April 2006 and March 2020. At this visit, we, first, recorded maternal demographic characteristics and medical history, as reported by the patients, second, carried out an ultrasound examination of fetal anatomy and measurement of fetal head circumference, abdominal circumference and femur length to calculate EFW using the Hadlock formula[12], identified as the most accurate model in a systematic review[13], third, measured MAP by validated automated devices according to a standardized protocol[14] and, fourth, measured left and right UtA-PI using either transvaginal or transabdominal color Doppler ultrasound and calculated the mean value of the two arteries[15,16]. The majority of UtA-PI measurements were carried out transvaginally because at the same time we were measuring cervical length; the transabdominal approach was used when women declined transvaginal sonography. Gestational age was determined from measurement of fetal crown–rump length at 11–13 weeks[17].

The inclusion criterion for this study was a singleton pregnancy that resulted in a phenotypically normal live birth or stillbirth at ≥ 24 weeks' gestation. Pregnancies with known aneuploidy or major fetal abnormality and those resulting in a miscarriage or termination of pregnancy were excluded.

Outcome measures

Outcome measures were delivery with PE at < 32 and < 37 weeks' gestation and at any gestational age. Data on pregnancy outcome were collected from the hospital maternity records or the general medical practitioners of the women. The obstetric records of all women with chronic hypertension or pregnancy-associated hypertension were examined to determine the diagnosis of PE. This was based on the finding of new-onset hypertension (systolic blood pressure of ≥ 140 mmHg or diastolic blood pressure of ≥ 90 mmHg on at least two occasions 4 h apart developing after 20 weeks' gestation in previously normotensive women) or chronic hypertension and at least one of the following: proteinuria (≥ 300 mg/24 h or protein-to-creatinine ratio ≥ 30 mg/mmol or ≥ 2+ on dipstick testing), renal insufficiency with serum creatinine > 97 μmol/L in the absence of underlying renal disease, hepatic dysfunction with blood concentration of transaminases more than twice the upper limit of normal (≥ 65 IU/L for our laboratory), thrombocytopenia (platelet count < 100 000/μL), neurological complications (e.g. cerebral or visual symptoms) or pulmonary edema[18].

Statistical analysis

Data were expressed as median (interquartile range (IQR)) for continuous variables and *n* (%) for categorical variables. Student's *t*-test and chi-square test or Fisher's exact test were used for comparing outcome groups for continuous and categorical data, respectively.

Fetal weight was estimated using the Hadlock 3 formula[12], and the Fetal Medicine Foundation fetal and neonatal population-weight charts were used to calculate EFW and birth-weight *Z*-scores[19]. The distribution of birth-weight *Z*-scores for pregnancies delivering with PE according to gestational age at delivery, pregnancies delivering with gestational hypertension (GH) and those unaffected were assessed using boxplots. Similar boxplots for EFW and a scatterplot of EFW *Z*-scores against gestational age at delivery with PE were produced. The relationship between EFW *Z*-score and gestational age at delivery with PE was assumed to be linear, up until the mean EFW *Z*-score of zero. Beyond this point, and for unaffected pregnancies, the mean was assumed to be zero. Correlations between the EFW *Z*-score and MAP and UtA-PI were also calculated.

The competing-risks model was used to estimate the individual patient-specific risk of delivery with PE at < 32 and < 37 weeks' gestation and at any gestational age by a combination of maternal demographic characteristics and medical history with biomarkers[20]. The competing-risks approach is based on a survival-time model for gestational age at delivery with PE. In our approach, we assumed that, if the pregnancy was to continue indefinitely, all women would develop PE and whether they do so or not before a specified gestational age depends on competition between delivery before or after development of PE.

The posterior distribution of gestational age at delivery with PE was obtained using Bayes' theorem by multiplying

the prior probability density from maternal factors by the likelihood function from biomarker MoM values and *Z*-scores. The measured values of biomarkers were converted to MoMs or *Z*-scores to remove the effects of characteristics such as gestational age, weight, race, method of conception, medical conditions, obstetric history of the individual and characteristics of the instrument used for the measurement. The areas under the receiver-operating-characteristics curves (AUC) and detection rates (DRs) of delivery with PE, at a 10% false-positive rate (FPR), were assessed for various combinations of maternal risk factors, EFW, MAP and UtA-PI. McNemar's test was used to determine the significance of difference in DR at 10% FPR of screening with and without EFW.

The statistical software package R was used for data analysis[21].

RESULTS

Study participants

The study population of 93 911 pregnancies contained 2843 (3.0%) pregnancies that subsequently developed PE, including 148 (0.2%) that delivered with PE at < 32 weeks' gestation and 654 (0.7%) that delivered with PE at < 37 weeks; in addition, there were 2663 (2.8%) cases that developed GH. The characteristics of the study population are summarized in Table 1. In the PE group, compared with unaffected pregnancies, there was a higher median weight and body mass index, higher incidence of women of black racial origin, those with a history of chronic hypertension and diabetes mellitus, family history of PE, conception by *in-vitro* fertilization, nulliparous women and parous women with history of PE and longer interpregnancy interval.

Birth-weight distribution in pre-eclampsia and unaffected pregnancies

The distribution of birth-weight *Z*-score according to gestational age at delivery with PE, GH and no PE or GH is shown in Figure 1a. In the PE group, birth-weight *Z*-score increased with gestational age at delivery. In both PE and unaffected pregnancies, the incidence of SGA neonate with birth weight < 10th percentile decreased with increasing gestational age at delivery (Figure 1b). The incidence of SGA decreased from 82.4% (122/148) for pregnancies with PE delivering at < 32 weeks' gestation to 20.6% (450/2189) for pregnancies with PE delivering at ≥ 37 weeks. The respective values for unaffected pregnancies were 33.1% (286/864) and 10.9% (11 520/105 337).

Estimated fetal weight distribution in pre-eclampsia and unaffected pregnancies

The distribution of EFW *Z*-score according to gestational age at delivery with PE, GH and no PE or GH is shown in Figure 2a. In the PE group, the EFW *Z*-score increased with gestational age at delivery. The fitted relationship between EFW *Z*-score and gestational age at delivery with PE is shown in Figure 2b (intercept, −9.7012 (95% CI, −0.6407 to −6.2003); slope, 0.2812 (95% CI, 0.1723–0.3094)). The EFW *Z*-score was low in pregnancies delivering with PE and increased with gestational age at delivery. According to our model, the average EFW *Z*-score for pregnancies delivering with PE after 34.5 weeks is assumed to be zero. The correlation coefficient was −0.0085 (95% CI, −0.0160 to −0.0010) ($P = 0.009$) between EFW *Z*-score and $\log_{10}$ MAP MoM and −0.0110 (95% CI, −0.0185 to −0.0035) ($P < 0.0001$) between EFW *Z*-score and $\log_{10}$ UtA-PI MoM.

Performance of screening for pre-eclampsia

The AUCs and DRs, at 10% FPR, in screening for delivery with PE at < 32 and < 37 weeks' gestation and at any gestational age by maternal risk factors and combinations of EFW, MAP and UtA-PI are shown in Tables 2 and 3.

Table 1 Maternal and pregnancy characteristics of the study population of 93 911 pregnancies, according to development of pre-eclampsia (PE)

Characteristic	*No PE (n = 91 068)*	*PE (n = 2843)*	P
Age (years)	31.5 (27.2–35.1)	31.5 (27.0–35.4)	0.982
Weight (kg)	71.5 (63.7–82.5)	78.0 (68.0–92.5)	< 0.0001
BMI (kg/m^2)	26.3 (23.5–30.1)	28.0 (25.3–34.0)	< 0.0001
GA (weeks)	21.7 (21.1–22.3)	21.9 (21.1–22.3)	0.980
Racial origin			< 0.0001
White	67 206 (73.8)	1809 (63.6)	
Black	15 001 (16.5)	823 (28.9)	
South Asian	4398 (4.8)	113 (4.0)	
East Asian	1803 (2.0)	36 (1.3)	
Mixed	2660 (2.9)	62 (2.2)	
Medical history			
Chronic hypertension	847 (0.9)	331 (11.6)	< 0.0001
DM Type I	370 (0.4)	32 (1.1)	< 0.0001
DM Type II	590 (0.6)	54 (1.9)	< 0.0001
SLE/APS	209 (0.2)	11 (0.4)	0.130
Smoker	7546 (8.3)	152 (5.3)	< 0.0001
Family history of PE	3534 (3.9)	228 (8.0)	< 0.0001
Method of conception			< 0.0001
Spontaneous	87 706 (96.3)	2675 (94.1)	
In-vitro fertilization	2685 (2.9)	142 (5.0)	
Ovulation drugs	677 (0.7)	26 (0.9)	
Parity			< 0.0001
Nulliparous	41 608 (45.7)	1745 (61.4)	
Parous, no previous PE	47 220 (51.9)	762 (26.8)	
Parous, previous PE	2240 (2.5)	336 (11.8)	
Interpregnancy interval (years)	2.9 (1.8–4.7)	3.7 (2.2–6.4)	< 0.0001

Data are given as median (interquartile range) or *n* (%). APS, anti-phospholipid syndrome; BMI, body mass index; DM, diabetes mellitus; GA, gestational age; SLE, systemic lupus erythematosus.

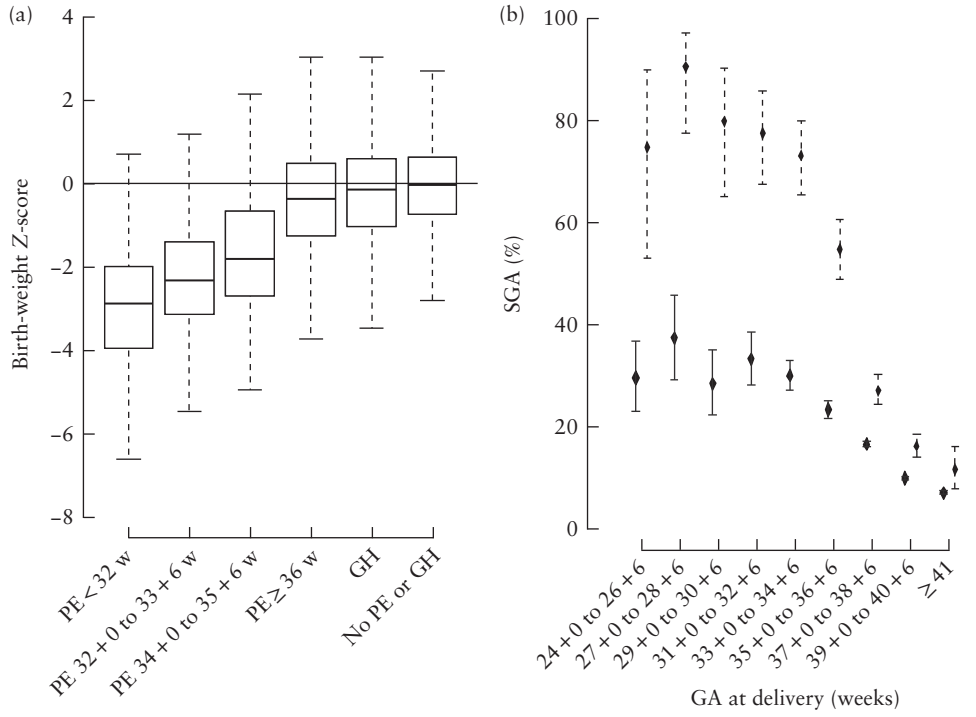

Figure 1 (a) Boxplots showing birth-weight *Z*-score distribution according to gestational age (GA) at delivery with pre-eclampsia (PE), gestational hypertension (GH) and no PE or GH. Boxes show median and interquartile range and whiskers are range. (b) Proportion of small-for-gestational-age (SGA) cases plotted against GA at delivery with PE (- - - -) and without PE (——) with 95% CI. w, weeks.

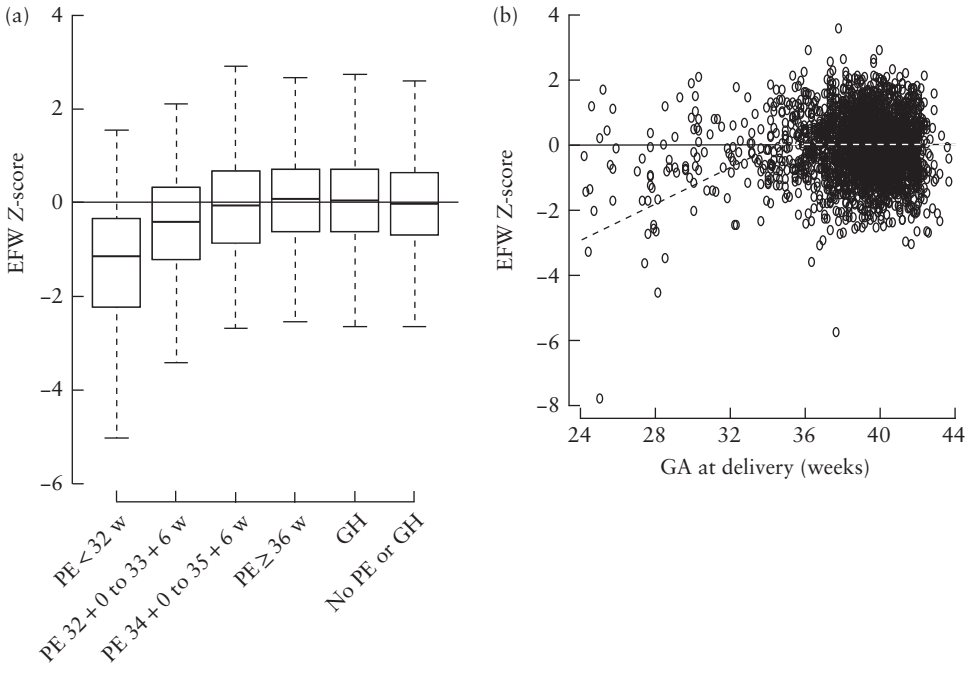

Figure 2 (a) Boxplots showing estimated-fetal-weight (EFW) *Z*-score distribution according to gestational age (GA) at delivery with pre-eclampsia (PE), gestational hypertension (GH) and no PE or GH. Boxes show median and interquartile range and whiskers are range. (b) EFW *Z*-score plotted against GA at delivery with PE. The dashed line indicates the fitted relationship. w, weeks.

In screening for delivery with PE at < 32 and < 37 weeks' gestation, the DRs, at 10% FPR, achieved by maternal risk factors (51.4% and 46.3%, respectively) were improved by addition of EFW (68.9% and 50.8%, respectively). Similarly, addition of EFW improved the performance of screening by a combination of maternal risk factors and MAP from 72.3% to 79.7% for PE < 32 weeks and from 57.2% to 59.5% for PE < 37 weeks. EFW did not improve the predictive performance of screening by a combination of maternal risk factors, MAP and UtA-PI.

Table 2 Areas under receiver-operating-characteristics curves for mid-gestation screening by maternal factors (MF) and combinations of estimated fetal weight (EFW), uterine artery pulsatility index (UtA-PI) and mean arterial pressure (MAP) for pre-eclampsia (PE) with delivery at < 32 and < 37 weeks' gestation and all PE

Method of screening	*PE < 32 weeks*	*PE < 37 weeks*	*All PE*
MF	0.811 (0.778–0.845)	0.801 (0.785–0.818)	0.746 (0.737–0.755)
MF + EFW	0.885 (0.857–0.913)	0.816 (0.800–0.833)	0.747 (0.738–0.756)
MF + MAP	0.909 (0.887–0.931)	0.852 (0.838–0.866)	0.790 (0.782–0.799)
MF + MAP + EFW	0.936 (0.919–0.954)	0.859 (0.845–0.873)	0.791 (0.783–0.799)
MF + UtA-PI	0.968 (0.957–0.979)	0.901 (0.887–0.914)	0.777 (0.768–0.786)
MF + UtA-PI + EFW	0.976 (0.968–0.984)	0.902 (0.889–0.915)	0.777 (0.768–0.786)
MF + MAP + UtA-PI	0.977 (0.967–0.987)	0.916 (0.903–0.928)	0.811 (0.802–0.819)
MF + MAP + UtA-PI + EFW	0.983 (0.976–0.990)	0.916 (0.904–0.928)	0.811 (0.803–0.819)

Values in parentheses are 95% CI.

DISCUSSION

Main findings

There are four main findings of this large screening study. First, the incidence of SGA in pregnancies complicated by PE is related inversely to gestational age at delivery, decreasing from 82% in those delivering at < 32 weeks to 21% in those delivering at ≥ 37 weeks. Second, in pregnancies without PE, there is an inverse association between the incidence of SGA neonate and gestational age at delivery, with the incidence decreasing from 33% in those delivering at < 32 weeks to 11% in those delivering at ≥ 37 weeks. Third, EFW measured at mid-gestation is a useful biomarker for subsequent development of preterm PE. ln screening for delivery with PE at < 32 and < 37 weeks' gestation, the DRs, at 10% FPR, achieved by maternal risk factors (51% and 46%, respectively) were improved by addition of EFW (69% and 51%, respectively). Similarly, addition of EFW

Table 3 Detection rates (DR), at a 10% false-positive rate (FPR), of pre-eclampsia (PE) with delivery at < 32 and < 37 weeks' gestation and all PE, for mid-gestation screening by maternal factors and combinations of estimated fetal weight (EFW), uterine artery pulsatility index (UtA-PI) and mean arterial pressure (MAP)

Method of screening	*Detected* (n/N)	*DR at 10% FPR (%) (95% CI)*	*Difference in DR (%) (95% CI)*	P
PE < 32 weeks ($n = 148$)				
Maternal factors	76/148	51.4 (43.0–59.6)	17.6 (9.5–25.9)	0.0001
Maternal factors + EFW	102/148	68.9 (60.8–76.3)		
Maternal factors + MAP	107/148	72.3 (64.3–79.3)	7.4 (0.9–14.5)	0.046
Maternal factors + MAP + EFW	118/148	79.7 (72.3–85.9)		
Maternal factors + UtA-PI	138/148	93.2 (87.9–96.7)	0 (−3.1 to 3.1)	1.000
Maternal factors + UtA-PI + EFW	138/148	93.2 (87.9–96.7)		
Maternal factors + MAP + UtA-PI	140/148	94.6 (89.6–97.6)	2.0 (−1.3 to 6.2)	0.371
Maternal factors + MAP + UtA-PI + EFW	143/148	96.6 (92.3–98.9)		
PE < 37 weeks ($n = 654$)				
Maternal factors	303/654	46.3 (42.5–50.2)	4.4 (2.2–6.9)	0.0003
Maternal factors + EFW	332/654	50.8 (46.9–54.7)		
Maternal factors + MAP	374/654	57.2 (53.3–61.0)	2.3 (0.5–4.3)	0.021
Maternal factors + MAP + EFW	389/654	59.5 (55.6–63.3)		
Maternal factors + UtA-PI	494/654	75.5 (72.1–78.8)	0.8 (−0.2 to 1.9)	0.182
Maternal factors + UtA-PI + EFW	499/654	76.3 (72.8–79.5)		
Maternal factors + MAP + UtA-PI	514/654	78.6 (75.2–81.7)	−0.2 (−1 to 0.6)	1.000
Maternal factors + MAP + UtA-PI + EFW	513/654	78.4 (75.1–81.5)		
All PE ($n = 2843$)				
Maternal factors	1041/2843	36.6 (34.8–38.4)	0.2 (−0.3 to 0.8)	0.419
Maternal factors + EFW	1048/2843	36.9 (35.1–38.7)		
Maternal factors + MAP	1236/2843	43.5 (41.6–45.3)	0.2 (−0.2 to 0.6)	0.458
Maternal factors + MAP + EFW	1241/2843	43.7 (41.8–45.5)		
Maternal factors + UtA-PI	1283/2843	45.1 (43.3–47.0)	0 (−0.4 to 0.4)	1.000
Maternal factors + UtA-PI + EFW	1283/2843	45.1 (43.3–47.0)		
Maternal factors + MAP + UtA-PI	1442/2843	50.7 (48.9–52.6)	0.3 (0–0.6)	0.118
Maternal factors + MAP + UtA-PI + EFW	1450/2843	51.0 (49.1–52.9)		

McNemar's test was used to determine statistical significance of difference in DR, at a 10% FPR, between screening with *vs* without EFW.

improved the performance of screening by a combination of maternal risk factors and MAP from 72% to 80% for PE < 32 weeks and from 57% to 60% for PE < 37 weeks. Fourth, EFW did not improve the predictive performance of screening for early PE and preterm PE by a combination of maternal risk factors, MAP and UtA-PI.

Interpretation of results

The mechanism underlying PE and SGA is thought to involve impaired trophoblastic invasion of the maternal spiral arteries and their conversion from narrow muscular vessels to wide non-muscular channels[22,23]. Our findings suggest that there is a wide spectrum of such impaired placentation, with severe impairment leading to early PE with SGA and less severe impairment causing late PE without SGA. The inverse association between incidence of SGA and gestational age at delivery with PE is consistent with the finding of pathological studies that the prevalence of placental lesions in women with PE is related inversely to gestational age at delivery[24,25].

The finding that, even in pregnancies without PE, a high proportion of preterm births are SGA is consistent with the fact that, first, in many such cases, there is iatrogenic birth for fetal growth restriction and, second, in many cases of spontaneous preterm birth, there is histological and uterine artery Doppler evidence of impaired placentation[26–30].

Comparison with findings of previous studies

Our finding that, in pregnancies with PE, there is an inverse association between the incidence of SGA neonate and gestational age at delivery is consistent with the results of several previous studies. The only previous study that provided detailed breakdown on the relationship between PE and SGA for each gestational age at delivery was that of Yu *et al.*,[9] and our results are very similar. This is the first study examining the potential value of EFW at mid-gestation in the prediction of PE.

In a case–control study of 307 cases of PE and 619 controls, Odegard *et al.* reported that the incidence of SGA was 53% in the early PE group (< 32 weeks) compared with 7.4% in the late PE group (≥ 32 weeks)[1]. In a population study of 87 798 pregnancies with data collected from 35 hospitals in the USA, Xiong *et al.* found that, for women delivering at ≤ 37 weeks, birth weight was significantly lower among women with PE than among women without PE, whereas, for women delivering at > 37 weeks, the mean birth weight was similar between women with and those without PE[2]. In a cohort study of 5725 singleton pregnancies, including 155 cases with PE, Xiao *et al.* reported that the incidence of SGA was 36.5% in the preterm PE group (< 37 weeks) compared with 10.7% in the term PE group (≥ 37 weeks)[3]. In a study by Lisonkova and Joseph of 456 668 singleton deliveries in Washington State, 2003–2008, including 1752 with early PE (< 34 weeks) and 12 449 with late PE (≥ 34 weeks), the incidence of SGA was 32.1% in the early PE compared with 16.1% in the late PE group[4]. In a cohort study of 44 cases of early PE (< 34 weeks) and 24 of late PE (≥ 34 weeks), Stubert *et al.* reported that the incidence of SGA was 34.1% and 20.8%, respectively[5]. Hung *et al.*, in a study of 19 494 singleton pregnancies, including 594 cases with PE, reported that the incidence of SGA was 50.5% in those with early PE (< 34 weeks) and 25.5% in those with late PE (≥ 34 weeks)[6]. Proctor *et al.*, in a study of 48 943 singleton pregnancies, including 1992 with hypertensive disorders of pregnancy (HDP), reported that the incidence of SGA in the group with HDP was 16.6% compared with 7.4% in those without HDP; the risk was more pronounced in the group with HDP delivering at < 34 weeks' gestation (30.7%)[7]. Liu *et al.* conducted a large cohort study of 201 000 singleton pregnancies in Chinese women, in which the incidence of SGA was 11% in the PE group and 6% in the normal group; the incidence of SGA was 17% in those with early PE (< 28 weeks) compared with 11% in those with late PE (≥ 28 weeks)[8].

Implications for clinical practice

We advocate screening for PE at around 12, 20 and 36 weeks' gestation. Screening at 12 weeks and treatment of the high-risk group with aspirin reduces the rate of preterm PE but has no significant effect on the incidence of term PE[31–36]. The rationale for second- and third-trimester screening[10,37–43] is identification of a high-risk group that would benefit from close monitoring to minimize the risk of adverse perinatal events for those that develop PE by determining the appropriate time and place for delivery. Assessment of risk for term PE is best carried out at 36 weeks' gestation because the performance of screening at 12, 20 or 32 weeks is poor. Useful biomarkers for preterm PE at the 20-week assessment include UtA-PI, MAP, placental growth factor (PlGF) and soluble fms-like tyrosine kinase-1 (sFlt-1). Measurement of MAP is part of routine assessment during pregnancy and measurement of UtA-PI can be carried out within a couple of minutes by the same sonographer and machine used for the routine second-trimester scan at minimum cost. In contrast, there are cost implications for measurement of PlGF and sFlt-1. Measurement of EFW is an integral part of the routine scan and, as shown in this study, can be useful for the prediction of preterm PE if UtA-PI is not measured. For example, in the UK, UtA-PI is not measured routinely during the mid-trimester scan.

Strengths and limitations

The main strength of the study is the prospective examination of a large number of pregnancies, including recording of relevant maternal risk factors and measurements of MAP and UtA-PI during the routine mid-trimester scan. The derived model for prediction of preterm PE incorporating the measurement of EFW requires validation.

Conclusions

In pregnancies complicated by preterm PE, a high proportion of neonates are SGA. Sonographic EFW at mid-gestation can improve the prediction of early and preterm PE provided by maternal risk factors and MAP but not the prediction provided by a combination of maternal risk factors, MAP and UtA-PI.

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