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Prediction of small-for-gestational-age neonates: screening by fetal biometry at 35–37 weeks

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KEYWORDS: abdominal circumference; estimated fetal weight; fetal biometry; pre-eclampsia; pyramid of antenatal care; small-for-gestational age; third-trimester screening

ABSTRACT

Objective *To investigate the value of fetal biometry at 35–37 weeks' gestation in the prediction of delivery of small-for-gestational-age (SGA) neonates, in the absence of pre-eclampsia (PE).*

Methods *This was a screening study in singleton pregnancies at 35–37 weeks' gestation, comprising 278 that delivered SGA neonates with a birth weight < 5th percentile and 5237 cases unaffected by SGA, PE or gestational hypertension. Multivariable logistic regression analysis was used to determine if screening by a combination of maternal factors and Z-scores of fetal head circumference (HC), abdominal circumference (AC) and femur length (FL) or estimated fetal weight (EFW) had a significant contribution to the prediction of SGA neonates.*

Results *Multivariable logistic regression analysis demonstrated that the likelihood of delivering a SGA neonate with a birth weight < 5th percentile decreased with maternal weight and height, and in parous women the risk increased with a longer interpregnancy interval. The risk was higher in women of Afro-Caribbean and South Asian racial origins, in cigarette smokers, nulliparous women and in those with history of SGA, with or without prior PE. Combined screening by maternal characteristics and history with EFW Z-scores at 35–37 weeks predicted 89% of SGA neonates with birth weight < 5th percentile delivering < 2 weeks following assessment, at a 10% false-positive rate (FPR). The respective detection rate for the prediction of SGA neonates delivering ≥ 37 weeks' gestation was 70%. The performance of screening by a combination of Z-scores of fetal HC, AC and FL was similar to that achieved by the EFW Z-score.*

Conclusion *Combined testing by maternal characteristics and fetal biometry at 35–37 weeks could identify, at a 10% FPR, about 90% of pregnancies that subsequently deliver SGA neonates within 2 weeks of assessment and 70% of those that deliver ≥ 37 weeks.* *Copyright © 2015 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

The increased risk of perinatal mortality and morbidity associated with small-for-gestational-age (SGA) neonates can be reduced substantially in cases identified prenatally, as close monitoring, timely delivery and prompt neonatal care can be undertaken[1].

A few studies comprising low-risk singleton pregnancies have examined the potential value of sonographic fetal biometry during the third trimester in the prediction of SGA neonates[2–8]. Three studies each examined a range of 725 to 1000 pregnancies at 26–36 weeks' gestation and reported that the estimated fetal weight (EFW) predicted 54–63% of SGA neonates with birth weight < 10th percentile, at a false-positive rate (FPR) of 20%[2–4]. Di Lorenzo *et al.*[5] assessed EFW at 30–32 weeks in the prediction of SGA neonates < 10th percentile in 1868 pregnancies, and reported that the detection rate (DR) was 73% at a FPR of 25%. Souka *et al.*[6] assessed EFW at 30–33 weeks in 2310 pregnancies and reported that, at a FPR of 10%, the DR of SGA neonates with birth weight < 5th percentile was 60%. Only one study examined the value of EFW in a late third-trimester ultrasound examination in low-risk pregnancies; EFW at 34–37 weeks' gestation in 2288 pregnancies predicted 75% of SGA neonates with birth weight < 5th percentile, at a FPR of 10%, which was superior to the DR of 58% in 3690 pregnancies examined at 30–33 weeks[7].

We have reported recently our findings from a screening study at 30–34 weeks in 30 849 singleton pregnancies[8]. Combined screening by maternal characteristics and history with EFW Z-scores predicted 79%, 87% and 92%

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of SGA neonates in the absence of PE delivering < 5 weeks following assessment with birth weights < 10^{th}, < 5^{th} and < 3^{rd} percentiles, respectively, at a 10% FPR. The respective DRs for prediction of SGA neonates delivering ≥ 5 weeks following assessment were 53%, 58% and 61%. Consequently, the performance of screening for SGA at 30–34 weeks is acceptably high for those delivering preterm, but disappointingly low for those delivering at term.

The objectives of this study in a large cohort of singleton pregnancies undergoing routine antenatal care were, first, to investigate the potential value of fetal biometry at 35–37 weeks' gestation in the prediction of delivery of SGA neonates in the absence of PE, and second, to combine these biomarkers with maternal characteristics and history to develop specific algorithms for the calculation of patient-specific risks for SGA.

METHODS

The data for this study were derived from prospective screening for adverse obstetric outcome in women attending for their routine hospital visit in the third trimester of pregnancy at King's College Hospital, London, and Medway Maritime Hospital, Kent, between February 2014 and September 2014. This visit, which was held at 35 + 0 to 37 + 6 weeks' gestation, included recording of maternal factors and EFW[9] from transabdominal ultrasound measurement of the fetal head circumference (HC), abdominal circumference (AC) and femur length (FL)[10], and measurement of uterine artery pulsatility index, mean arterial pressure and maternal serum metabolites. Gestational age was determined by the measurement of fetal crown–rump length at 11–13 weeks or fetal head circumference at 19–24 weeks[10,11].

Written informed consent was obtained from the women agreeing to participate in this study on adverse pregnancy outcome, which was approved by the ethics committee of each participating hospital. This study is part of a research program on the late third-trimester prediction of PE and/or SGA. In this study, we present the results on combined screening with maternal factors and fetal biometry in the prediction of SGA in the absence of PE. The pregnancies included in this study all resulted in live birth or the stillbirth of phenotypically normal babies.

Patient characteristics

Patient characteristics that were recorded included maternal age, racial origin (Caucasian, Afro-Caribbean, South Asian, East Asian and mixed), method of conception (spontaneous/assisted conception requiring the use of ovulation drugs), cigarette smoking during pregnancy (yes/no), medical history of chronic hypertension (yes/no), diabetes mellitus (yes/no), systemic lupus erythematosus (SLE) or antiphospholipid syndrome (APS), obstetric history including parity (parous/nulliparous if no previous pregnancy ≥ 24 weeks' gestation), previous pregnancy with PE (yes/no), previous pregnancy with SGA (yes/no) and the time interval (years) between last delivery and conception of the current pregnancy. Maternal weight and height were also measured.

Outcome measures

Data on pregnancy outcomes were collected from the hospital maternity records or the general medical practitioners of the women. The primary outcome of the study was SGA without PE. The newborn was considered to be SGA if the birth weight was < 5^{th} percentile after correction for gestational age at delivery (SGA < 5^{th})[12]. The definitions of non-proteinuric gestational hypertension (GH) and PE were those of the International Society for the Study of Hypertension in Pregnancy[13]. The obstetric records of all women with pre-existing or pregnancy-associated hypertension were examined to confirm if the condition was chronic hypertension, PE or GH.

Statistical analysis

The observed measurements of fetal HC, AC, FL and EFW were expressed as the respective *Z*-score and percentile, corrected for gestational age[9,10]. Mann–Whitney *U*-test was used to compare the *Z*-scores of HC, AC, FL and EFW between the SGA and unaffected groups. Regression analysis was used to determine the significance of association between HC *Z*-score, AC *Z*-score, FL *Z*-score and EFW *Z*-score with the time interval between assessment and delivery.

The *a-priori* risk for SGA < 5^{th} were calculated using multivariable logistic regression analysis with backward stepwise elimination to determine which of the factors among maternal characteristics and obstetric history had a significant contribution in predicting SGA < 5^{th}.

Multivariable logistic regression analysis was used to determine if the maternal factor-derived logit (*a-priori* risk), HC *Z*-score, AC *Z*-score, FL *Z*-score or EFW *Z*-score had significant contribution in predicting SGA < 5^{th}. The performance of screening was determined by receiver–operating characteristics (ROC) curves. Similarly, the algorithm was used to determine the performance of screening for SGA defined by birth weight < 10^{th} percentile (SGA < 10^{th}) and birth weight < 3^{rd} percentile (SGA < 3^{rd}).

The statistical software package SPSS 22.0 (SPSS Inc., Chicago, IL, USA) and Medcalc (Medcalc Software, Mariakerke, Belgium) were used for all data analyses.

RESULTS

The study population comprised of 5515 pregnancies, including 278 (5.0%) that delivered SGA < 5^{th} neonates in the absence of PE and 5237 (95.0%) cases that were unaffected by these outcomes. The characteristics of the study population are given in Table 1. In the SGA group, compared with the normal group, there was a lower median maternal weight and height, a higher prevalence of South Asian racial origin, nulliparous women, parous women

Table 1 Characteristics of the study population of pregnant women with normal outcomes and those with small-for-gestational-age (SGA) neonates without pre-eclampsia (PE)

Characteristic	*Normal* (n = *5237*)	*SGA without PE* (n = *278*)	P
Maternal age (years)	31.2 (26.5–35.0)	30.1 (24.8–35.3)	0.067
Maternal weight (kg)	79.0 (70.9–89.9)	73.2 (64.2–83.5)	< 0.0001
Maternal height (cm)	164 (160–168)	162 (157–165)	< 0.0001
GA at screening (weeks)	36.1 (36.0–36.4)	36.3 (36.0–36.4)	0.916
Racial origin			
Caucasian	3720 (71.0)	161 (57.9)	< 0.0001
Afro-Caribbean	1034 (19.7)	64 (23.0)	0.190
South Asian	199 (3.8)	34 (12.2)	< 0.0001
East Asian	109 (2.1)	6 (2.2)	0.830
Mixed	175 (3.3)	13 (4.7)	0.233
Obstetric history			
Nulliparous	2537 (48.4)	172 (61.9)	0.001
Parous with no prior PE or SGA	2481 (47.4)	73 (26.3)	< 0.0001
Parous with prior PE, no SGA	82 (1.6)	5 (1.8)	0.459
Parous with prior SGA, no PE	127 (2.4)	27 (9.7)	0.002
Parous with prior SGA and PE	10 (0.2)	1 (0.4)	> 0.999
Interpregnancy interval (years)	3.1 (2.1–5.1)	2.9 (2.1–5.5)	0.965
Cigarette smoker	503 (9.6)	62 (22.3)	< 0.0001
Mode of conception			
Spontaneous	5110 (97.6)	266 (95.7)	0.072
Ovulation drugs	23 (0.4)	2 (0.7)	0.362
In-vitro fertilization	104 (2.0)	10 (3.6)	0.079
Chronic hypertension	72 (1.4)	2 (0.7)	0.588
Pre-existing diabetes mellitus	65 (1.2)	3 (1.1)	> 0.999
Type 1	31 (0.6)	2 (0.7)	> 0.999
Type 2	34 (0.6)	1 (0.4)	> 0.999
SLE or APS	13 (0.2)	0 (0.0)	> 0.999
GA at delivery (weeks)	40.0 (39.0–40.9)	39.4 (38.4–40.4)	< 0.0001
Birth weight (g)	3430 (3140–3745)	2550 (2347–2721)	< 0.0001
Birth-weight percentile	50.3 (26.6–75.6)	2.7 (1.2–3.7)	< 0.0001

Data are given as median (interquartile range) or *n* (%). APS, antiphospholipid syndrome; GA, gestational age; SLE, systemic lupus erythematosus.

with a history of SGA and cigarette smokers, and a lower prevalence of Caucasian racial origin and parous women with no history of SGA and PE. The median gestational age at delivery and neonatal birth weight were significantly lower in the SGA group than in the normal group.

There were significant ($P < 0.0001$) intercorrelations between *Z*-score values of HC, AC and FL in both the SGA and normal outcome groups with *r*-values ranging from 0.146 to 0.381.

Normal pregnancy outcome

There was a significant linear association between HC *Z*-score and the assessment-to-delivery interval ($-0.298 + (0.040 \times$ delivery interval); $r = 0.087$; $P < 0.0001$) and between EFW *Z*-score and the assessment-to-delivery interval ($0.281 + (0.025 \times$ delivery interval); $r = 0.047$; $P = 0.001$), and there was a significant polynomial association between AC *Z*-score and the assessment-to-delivery interval ($-0.146 + (0.077 \times$ delivery interval) $- (0.010 \times$ delivery interval^2); $r = 0.040$; $P = 0.015$) and between FL *Z*-score and the assessment-to-delivery interval ($-0.215 + (0.194 \times$ delivery interval) $- (0.053 \times$ delivery interval^2) $+ (0.005 \times$ delivery interval^3); $r = 0.043$; $P = 0.022$).

Small-for-gestational age

In the SGA < 5th group, the median *Z*-score values of HC, AC, FL and EFW at 35–37 weeks were significantly lower ($P < 0.0001$) than those of the normal group. There was a significant linear association between HC *Z*-score and the assessment-to-delivery interval ($-1.147 + (0.098 \times$ delivery interval); $r = 0.249$; $P < 0.0001$; Figure S1a); AC *Z*-score and assessment-to-delivery interval ($-1.684 + (0.214 \times$ delivery interval); $r = 0.481$; $P < 0.0001$; Figure S1b); FL *Z*-score and assessment-to-delivery interval ($-1.263 + (0.190 \times$ delivery interval); $r = 0.314$; $P < 0.0001$; Figure S1c); and EFW *Z*-score and assessment-to-delivery interval ($-1.572 + (0.234 \times$ delivery interval); $r = 0.505$; $P < 0.0001$; Figure S1d).

The *a-priori* risk for SGA < 5th is calculated from the following formula: odds/(1 + odds), where odds = e^Y and Y is derived from multivariable logistic regression analysis. Regression coefficients and adjusted odds ratios of each of the maternal factors in the prediction algorithms are presented in Table 2 ($R^2 = 0.106$, $P < 0.0001$). The likelihood of SGA < 5th decreased with maternal weight and height, and in parous women the risk increased with interpregnancy interval. The risk was higher in women of Afro-Caribbean and South Asian racial origin, in

Table 2 Fitted regression model with maternal characteristics and history for the prediction of small-for-gestational age (SGA) with birth weight < 5th percentile in the absence of pre-eclampsia (PE)

Independent variable	*Coefficient*	*SE*	*OR (95% CI)*	P
Intercept	−0.89206	0.39700		
Weight (−75)*	−0.02012	0.01094	0.980 (0.970–0.990)	< 0.0001
Height (−165)†	−0.03839	0.01094	0.962 (0.942–0.983)	0.0004
Racial origin				
Caucasian, East Asian, mixed (reference)	0		1	
Afro-Caribbean	0.56782	0.15750	1.764 (1.296–2.403)	0.0003
South Asian	1.08597	0.21540	2.962 (1.942–4.518)	< 0.0001
Cigarette smoker	1.08264	0.16094	2.952 (2.154–4.047)	< 0.0001
Obstetric history				
Nulliparous	1.06018	0.16341	2.887 (2.096–3.977)	< 0.0001
Parous				
No previous SGA ± PE (reference)	−3.23409	0.17404	0.021	
Interpregnancy interval in years	0.06583	0.02655	1.081 (1.026–1.139)	0.003
Previous SGA ± PE	1.59429	0.23809	6.639 (4.163–10.587)	< 0.0001

*Subtracted from maternal weight in kg. †Subtracted from maternal height in cm. OR, odds ratio; SE, standard error.

cigarette smokers, nulliparous women and in those with a prior SGA pregnancy, with or without prior PE. The risk was lower in parous women with no history of SGA, with or without prior PE. The likelihood of SGA < 5th was not altered significantly by maternal age ($P = 0.911$), method of conception ($P = 0.083$), chronic hypertension ($P = 0.502$), diabetes mellitus ($P = 0.645$) and SLE or APS ($P = 0.998$).

Multivariable logistic regression analyses demonstrated that, in the prediction of SGA < 5th, there were significant contributions from maternal characteristics and a combination of HC *Z*-score, AC *Z*-score and FL *Z*-score or EFW *Z*-score ($R^2 = 0.407$, $P < 0.0001$; Table S1).

The areas under the ROC curves (AUC) and the DRs at FPRs of 5% and 10% and FPRs for DRs of 100%, 90% and 80% of SGA < 10th, SGA < 5th and SGA < 3rd, delivering < 2 weeks after assessment and ≥ 37 weeks' gestation, when screening by maternal characteristics and a combination of HC, AC and FL *Z*-scores or EFW *Z*-score are given in Tables 3, S2 and S3 and Figure 1.

Prediction of SGA delivering < 2 or ≥ 2 weeks following screening at 35–37 weeks

The DRs, at a FPR of 10%, of combined screening by maternal characteristics and history with EFW *Z*-scores for the prediction of SGA neonates with birth weight < 10th, < 5th and < 3rd percentiles, delivering ≥ 2 weeks following assessment, were 62.6% (95% CI, 58.3–66.7; AUC: 0.875 (95% CI, 0.866–0.884)), 67.1% (95% CI, 60.6–73.2; AUC: 0.895 (95% CI, 0.886–0.903)) and 74.4% (95% CI, 65.6–81.9; AUC: 0.916 (95% CI, 0.909–0.924)), respectively. The performance of screening was better for the prediction of SGA delivering within 2 weeks of assessment with respective DRs of 87.8% (95% CI, 79.6–93.5; AUC: 0.961 (95% CI, 0.955–0.966)), 88.7% (95% CI, 77.0–95.7; AUC: 0.972 (95% CI, 0.967–0.976)) and 91.7% (95% CI, 77.5–98.2); AUC: 0.983 (95% CI, 0.979–0.986)) (Tables 3 and S2).

Prediction of SGA delivering ≥ 37 weeks with screening at 35–37 compared to 30–34 weeks

In combined screening by maternal characteristics and history with EFW *Z*-scores at 35–37 weeks' gestation, the DRs, at a FPR of 10%, of SGA neonates with birth weight < 10th, < 5th and < 3rd percentiles delivering ≥ 37 weeks were 66.0% (95% CI, 62.0–69.7; AUC: 0.887 (95% CI, 0.879–0.895)), 70.0% (95% CI, 64.0–75.4; AUC: 0.906 (95% CI, 0.898–0.913)) and 77.2% (95% CI, 69.6–83.7; AUC: 0.928 (95% CI, 0.921–0.935)), respectively (Tables 3 and S3). Using data from our recent publication in combined screening by maternal characteristics and history with EFW *Z*-scores at 30–34 weeks[8], the respective DRs were 53.0% (95% CI, 51.3–54.8; AUC: 0.833 (95% CI, 0.829–0.837)), 58.3% (95% CI, 55.7–60.9; AUC: 0.859 (95% CI, 0.855–0.863)) and 60.8% (95% CI, 62.6–85.0; AUC: 0.875 (95% CI, 0.871–0.879)).

DISCUSSION

Main findings of the study

The findings of this study demonstrate that the risk for delivering SGA neonates in the absence of PE, increases with a longer interpregnancy interval, decreases with maternal weight and height, it is higher in women of Afro-Caribbean or South Asian racial origin than in Caucasian women, in cigarette smokers, nulliparous women and in parous women with a history of SGA.

In women who deliver SGA neonates in the absence of PE, the fetal HC, AC, FL and EFW at 35–37 weeks' gestation are reduced. The prediction of SGA provided by the fetal AC is superior to that of HC or FL, but inferior to that of the combination of the three measurements. The performance of screening by a combination of *Z*-scores for fetal HC, AC and FL is similar to that achieved by the EFW *Z*-score.

Combined screening by maternal characteristics and history with EFW *Z*-scores at 35–37 weeks predicted

Table 3 Performance of screening for small-for-gestational-age (SGA) neonates with birth weight < 10th, < 5th and < 3rd percentile, delivering within 2 weeks of assessment and ≥ 37 weeks' gestation, in the absence of pre-eclampsia, using maternal characteristics and history, fetal biometry or estimated fetal weight at 35–37 weeks' gestation

		DR (%)		*FPR (%)*		
Screening test	*AUC*	*FPR = 5%*	*FPR = 10%*	*DR = 100%*	*DR = 90%*	*DR = 80%*
SGA delivering < 2 weeks following assessment						
SGA < 10th percentile						
Maternal characteristics and history	0.735 (0.722–0.747)	26.5 (18.1–36.4)	41.8 (31.9–52.2)	98.4 (98.0–98.7)	71.0 (69.7–72.3)	52.1 (50.7–53.5)
Plus EFW Z-score	0.961 (0.955–0.966)	77.6 (68.0–85.4)	87.8 (79.6–93.5)	53.5 (52.1–54.9)	11.9 (11.0–12.8)	5.8 (5.1–6.5)
SGA < 5th percentile						
Maternal characteristics and history	0.804 (0.793–0.815)	35.9 (23.1–50.2)	50.9 (36.8–64.9)	73.6 (72.4–74.8)	57.9 (56.6–59.3)	44.8 (43.5–46.2)
Plus EFW Z–score	0.972 (0.967–0.976)	84.9 (72.4–93.3)	88.7 (77.0–95.7)	34.6 (33.3–35.9)	11.1 (10.2–12.0)	3.0 (2.5–3.5)
SGA < 3rd percentile						
Maternal characteristics and history	0.807 (0.796–0.818)	38.9 (23.1–56.5)	50.0 (32.9–67.1)	62.4 (61.1–63.7)	57.9 (56.6–59.3)	40.5 (39.1–41.8)
Plus EFW Z-score	0.983 (0.979–0.986)	91.7 (77.5–98.2)	91.7 (77.5–98.2)	17.1 (16.1–18.2)	3.8 (3.3–4.3)	0.9 (0.7–1.3)
SGA delivering ≥ 37 weeks' gestation						
SGA < 10th percentile						
Maternal characteristics and history	0.709 (0.697–0.721)	19.7 (16.6–23.1)	32.2 (28.5–36.1)	99.9 (99.8–99.9)	70.5 (69.2–71.7)	53.4 (52.0–54.8)
Plus EFW Z-score	0.887 (0.879–0.895)	46.9 (42.9–51.0)	66.0 (62.0–69.7)	88.5 (87.6–89.4)	32.9 (31.6–34.02)	19.5 (18.4–20.6)
SGA < 5th percentile						
Maternal characteristics and history	0.734 (0.722–0.746)	22.4 (17.5–28.0)	35.7 (29.9–41.9)	98.1 (97.7–98.5)	68.8 (67.5–70.0)	49.7 (48.3–51.0)
Plus EFW Z-score	0.906 (0.898–0.913)	53.6 (47.4–59.8)	70.0 (64.0–75.4)	83.4 (82.4–84.4)	25.0 (23.9–26.2)	13.5 (12.6–14.5)
SGA < 3rd percentile						
Maternal characteristics and history	0.772 (0.761–0.784)	24.8 (18.1–32.6)	37.6 (29.8–45.9)	90.7 (89.9–91.5)	56.3 (54.9–57.6)	41.7 (40.4–43.1)
Plus EFW Z-score	0.928 (0.921–0.935)	63.8 (55.5–71.5)	77.2 (69.6–83.7)	69.3 (68.0–70.5)	19.6 (18.5–20.7)	10.6 (9.8–11.5)

AUC, area under receiver–operating characteristics curve; DR, detection rate; EFW, estimated fetal weight; FPR, false-positive rate.

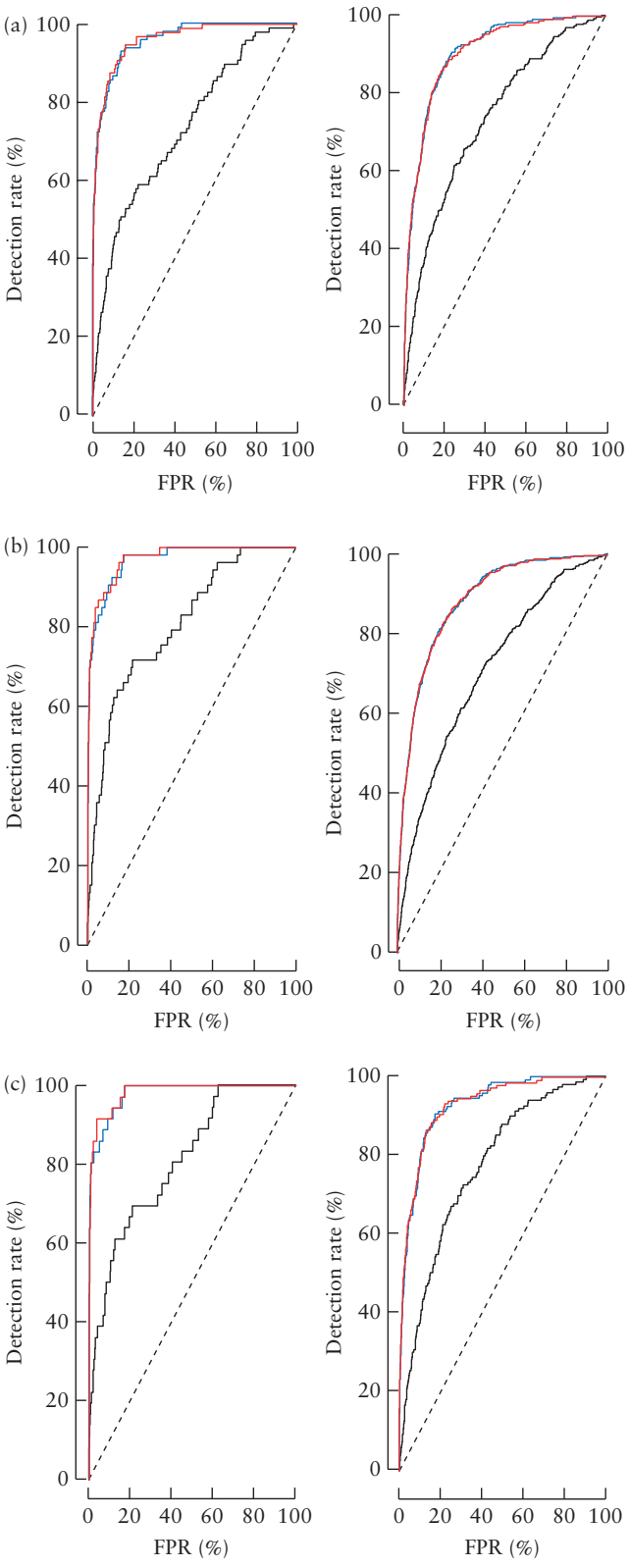

Figure 1 Receiver–operating characteristics curves of maternal characteristics (——), combination of maternal characteristics with fetal head circumference, abdominal circumference and femur length *Z*-score (——) and combination of maternal characteristics with estimated fetal weight *Z*-score (——) at 35–37 weeks' gestation in the prediction of small-for-gestational-age neonates with birth weight < 10th percentile (a), < 5th percentile (b) and < 3rd percentile (c), delivering < 2 weeks following assessment (left) or ≥ 37 weeks' gestation (right). FPR, false-positive rate.

about 70% of pregnancies that subsequently delivered SGA < 5th neonates ≥ 37 weeks, at a FPR of 10%. This was superior to the DR of 58% achieved by screening at 30–34 weeks[8]. The performance of screening was better in the prediction of SGA delivering within 2 weeks of assessment, with DR of about 90%.

Strengths and limitations of the study

The strengths of this third-trimester screening study for SGA in the absence of PE are first, examination of a population of pregnant women attending for routine assessment of fetal growth and wellbeing and second, use of Bayes' theorem to combine the prior risk from maternal characteristics and medical history with fetal biometry to estimate patient-specific risks and the performance of screening for SGA of different severities, delivering at term.

The main limitation of the study is that the results of the 35–37 weeks' scan were made available to the obstetricians of the patients who would have taken specific actions of further monitoring of the cases of suspected SGA. Consequently, the performance of screening would be positively biased.

Comparison with findings from previous studies

Our findings, that the prediction of SGA neonates with birth weight < 5th percentile at 35–37 weeks' gestation by sonographic estimation of EFW *Z*-scores is superior to that of screening at 30–34 weeks (70% *vs* 58%), at a FPR of 10%, are similar to those of a previous study that reported rates of 75% and 58% with screening at 34–37 and 30–33 weeks, respectively[7]. In the previous study[7], all cases of SGA were included, whereas in our study those associated with PE were excluded.

A routine third-trimester scan is by far superior to the traditional approach of abdominal palpation in identifying pregnancies at high risk of delivering SGA neonates. A population-based observational study of 6318 consecutive low-risk singleton pregnancies reported that abdominal palpation predicted only 21% and 28% of SGA neonates with birth weight < 10th and 2.3rd percentiles, respectively, at a FPR of about 5%[14]. One randomized study compared the effectiveness of serial measurements of symphysis–fundal height to that of abdominal palpation in the prediction of SGA neonates with birth weight < 10th percentile and reported no significant difference between the two methods (28% *vs* 48%, both at a FPR of about 4%)[15].

Implications for clinical practice

In the proposed new pyramid of pregnancy care[16], an integrated clinical assessment at 11–13 weeks' gestation, in which biophysical and biochemical markers are combined with maternal characteristics and medical history, aims to identify pregnancies at high risk of developing PE and/or SGA[17,18] and, through pharmacological intervention, reduce the prevalence of these complications[19,20].

The objectives of subsequent visits, at around 22 and 32 or 36 weeks' gestation, are to identify the high-risk group and, through close monitoring of such pregnancies, to minimize adverse perinatal events by determining the appropriate time and place for iatrogenic delivery. We found that screening at 32 weeks can identify, at a FPR of 10%, about 90% of SGA < 5th delivering preterm, but < 60% of those delivering at term[8]. Although a third-trimester scan at 36 weeks, rather than at 32 weeks, would improve the prediction of SGA < 5th delivering ≥ 37 weeks from 58% to 70%, this would be at the inevitable expense of missing preterm SGA. Future studies will investigate the extent to which selection of the timing of the third-trimester scan can be defined by the findings of screening at 12 and 22 weeks; women at high risk of early-onset SGA would be offered a scan at 32 weeks and those at low risk would be offered a scan at 36 weeks.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 *Z*-scores for fetal head circumference (HC) (a), abdominal circumference (AC) (b), femur length (FL) (c) and estimated fetal weight (EFW) (d) at 35–37 weeks' gestation, according to assessment-to-delivery interval, in pregnancies delivering small-for-gestational-age neonates with birth weight < 5th percentile. Horizontal solid and dashed lines indicate the 50th and 10th percentiles of the normal range. Red line indicates fitted mean from regression model.

Table S1 Fitted regression models with maternal characteristics and history, fetal head circumference *Z*-score, abdominal circumference *Z*-score, femur length *Z*-score or estimated fetal weight *Z*-score at 35–37 weeks' gestation, for the prediction of small-for-gestational age with birth weight < 5th percentile in the absence of pre-eclampsia.

Table S2 Detection rates in screening for small-for-gestational-age neonates with birth weight < 10th, < 5th or < 3rd percentile, delivering within 2 weeks of assessment, in the absence of pre-eclampsia, using maternal characteristics and history, fetal biometry or estimated fetal weight at 35–37 weeks' gestation.

Table S3 Detection rates in screening for small-for-gestational-age neonates with birth weight < 10th, < 5th or < 3rd percentile, delivering ≥ 37 weeks' gestation, in the absence of pre-eclampsia, using maternal characteristics and history, fetal biometry or estimated fetal weight at 35–37 weeks' gestation.

