**Prediction of small for gestational age neonates at 35-37 weeks' gestation:
Contribution of maternal factors and growth velocity between 20 and 36 weeks**

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Short title: Third trimester screening for SGA

Key words: Third trimester screening; Small for gestational age; Growth velocity; Estimated fetal weight; Pyramid of pregnancy care.

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ABSTRACT

Objective: To evaluate the performance of ultrasonographic estimated fetal weight (EFW) at 35^{+0} - 36^{+6} weeks' gestation in the prediction of small for gestational age (SGA) neonates and assess the additive value of first, maternal risk factors and second, fetal growth velocity between 20 and 36 weeks' gestation in improving such prediction.

Methods: This was a prospective study of 44,043 singleton pregnancies that had undergone routine ultrasound examination at 19^{+0} - 23^{+6} and at 35^{+0} - 36^{+6} weeks' gestation. Multivariable logistic regression analysis was used to determine whether addition of maternal risk factors and growth velocity, defined by a difference in EFW Z-scores or fetal abdominal circumference (AC) Z-scores between the third and second trimester scans divided by the time interval between them, improved the performance of EFW at 35^{+0} - 36^{+6} weeks in the prediction of delivery of SGA neonates with birthweight <10th and <3rd percentiles within two weeks and at any stage after assessment.

Results: Screening by EFW at 35^{+0} - 36^{+6} weeks' gestation <10th percentile predicted 63.4% (95% CI 62.0, 64.7) of neonates with birthweight <10th percentile and 74.2% (95% CI 72.2, 76.1) of neonates with birthweight <3rd percentile born at any stage after assessment, at screen positive rate of 10%. The respective values for SGA neonates born within two weeks of assessment were 76.8% (95% CI 74.4, 79.0) and 81.3% (95% CI 78.2, 84.0). In the group of fetuses with EFW <10th percentile, 43.7% were born with birthweight ≥10th percentile. For a desired 90% detection rate of SGA neonates delivering at any stage after assessment the necessary screen positive rate would be 33.7% for SGA <10th percentile and 24.4% for SGA <3rd percentile. Multivariable logistic regression analysis demonstrated that in the prediction of SGA neonates with birthweight <10th and <3rd percentiles there was a significant contribution from EFW Z-score at 35^{+0} - 36^{+6} weeks' gestation, maternal risk factors and AC growth velocity, but not EFW growth velocity. However, the area under the receiver operating characteristic curves for SGA neonates in screening by maternal risk factors and EFW Z-score was not improved by addition of AC growth velocity.

Conclusion: Screening for SGA neonates by EFW at 35^{+0} - 36^{+6} weeks' gestation and use of a cut-off of the 10th percentile predicts 63% of affected neonates. Prediction of 90% of SGA neonates necessitates classification of about 35% of the population as being screen positive use of the 35th percentile cut-off in EFW. The predictive performance of EFW is not improved by addition of estimated growth velocity between the second and third trimesters of pregnancy.

INTRODUCTION

Small for gestational age (SGA) neonates are at increased risk of perinatal mortality and both short- and long-term morbidity, but these risks can be reduced if the condition is identified prenatally, because in such cases close monitoring and appropriate timing of delivery and prompt neonatal care can be undertaken.[1-3] National guidelines from many developed countries define fetal growth restriction on the basis of ultrasonographic estimated fetal weight (EFW) <10th percentile and severe growth restriction as EFW <3rd percentile with recommendations on the time of delivery varying from 37 to 40 weeks' gestation depending on the severity of SGA and fetal Doppler findings.[4] However, there are several important issues that are often overlooked in such recommendations: first, the method of screening that leads to an ultrasound examination for estimation of fetal weight, second, the accuracy of such ultrasound examination, third, the selection of the reference ranges of EFW and birthweight for the diagnosis of SGA fetuses and SGA neonates, and fourth, the degree of fetal growth between assessment and delivery.

In this paragraph we summarize an approach for addressing the above issues. First, the traditional method of identifying pregnancies with SGA fetuses is maternal abdominal palpation and serial measurements of symphysial-fundal height, but the predictive performance of such screening is poor.[5,6] There is some evidence that substantially improved prediction of SGA is achieved by universal sonographic fetal biometry during the third trimester, especially at about 36 weeks' gestation;[7-11] this is because 85% of SGA neonates with birth weight <10th percentile are born at >37 weeks' gestation.[12] Second, a systematic review of 45 studies describing a total of 70 models for EFW by various combinations of measurements of fetal head circumference (HC), biparietal diameter, femur length (FL) and abdominal circumference (AC),[13] reported that the most accurate model was provided by the formula of Hadlock et al.,[14] which incorporated measurements of HC, AC and FL; the EFW measured within 2 days of delivery was within 10% of birth weight in 80% of cases.[13] Third, reference ranges of EFW are representative of the whole population, whereas in the construction of reference ranges of birthweight, particularly for gestational ages at <37 weeks, there is overrepresentation of pathological pregnancies; to overcome this problem we proposed the use of EFW and birth weight charts with a common median.[15] Fourth, in a previous study of 5,515 pregnancies undergoing routine ultrasound examination at 36 weeks' gestation we found that EFW <10th percentile predicted 87% of SGA neonates born within two weeks of assessment but only 63% of those born >37 weeks' gestation.[8] The study also reported that for a desired prediction of 90% of SGA neonates delivering >37 weeks the necessary screen positive rates would be about 35%.[8]

On the basis of the observed predictive performance for SGA neonates of EFW at 36 weeks' gestation, compliance with national guidelines on the diagnosis and management of SGA fetuses would necessitate intensive monitoring and / or early iatrogenic delivery of about 35% of pregnancies and accepting that we would still miss about 10% of SGA neonates.[8] The objectives of this expanded series of 44,043 singleton pregnancies are to evaluate the performance of EFW at 35^{+0} - 36^{+6} weeks' gestation in the prediction of SGA neonates and assess the additive value of first, maternal risk factors and second, fetal growth velocity between 20 and 36 weeks' gestation in improving such prediction.

METHODS

This was a prospective study of 44,043 singleton pregnancies that had undergone routine ultrasound examination at 19^{+0} - 23^{+6} and at 35^{+0} - 36^{+6} weeks' gestation at King's College Hospital, London or Medway Maritime Hospital, Gillingham, UK between October 2013 and September 2018. In the first visit we recorded maternal demographic characteristics and medical

history and in both visits we carried out an ultrasound examination for fetal anatomy and measurement of fetal HC, AC and FL for calculation of EFW.[14] Gestational age was determined by the measurement of fetal crown-rump length at 11-13 weeks or the fetal head circumference at 19-24 weeks.[16,17] The ultrasound examinations were carried out by 256 examiners who had obtained the Fetal Medicine Foundation certificate of competence in ultrasound examination for fetal abnormalities.

The women gave written informed consent to participate in the study, which was approved by the NHS Research Ethics Committee. The inclusion criteria for this study were singleton pregnancies examined at both 19^{+0} - 23^{+6} and at 35^{+0} - 36^{+6} weeks' gestation and delivering a non-malformed live birth or stillbirth. We excluded pregnancies with aneuploidies and major fetal abnormalities.

Patient characteristics

Patient characteristics recorded included maternal age, racial origin (White, Black, South Asian, East Asian and mixed), method of conception (natural, *in vitro* fertilization or use of ovulation induction drugs), cigarette smoking during pregnancy, medical history of chronic hypertension and diabetes mellitus, obstetric history including parity (parous or nulliparous if no previous pregnancies at $\geq$ 24 weeks' gestation), and previous pregnancy with SGA. The maternal weight and height were measured.

Outcome measures

Data on pregnancy outcome were collected from the hospital maternity records or the general medical practitioners of the women. The outcome measures of the study were birth of a neonate with birth weight <10th or <3rd percentile for gestational age at delivery.[14]

Statistical analysis

Data were expressed as median (interquartile range [IQR]) for continuous variables and n (%) for categorical variables. Mann-Whitney U-test and χ^2-square test or Fisher's exact test, were used for comparing outcome groups for continuous and categorical data, respectively. Significance was assumed at 5%.

In the dataset of 44,043 singleton pregnancies with paired measurements of fetal biometry examined at 19^{+0} - 23^{+6} and 35^{+0} - 36^{+6} weeks' gestation, the observed measurements of EFW and AC were expressed as Z-scores for gestational age.[14,17] The *a priori* risk for SGA based on maternal factors was derived from a dataset of 124,443 singleton pregnancies at 11^{+0} - 13^{+6} weeks' gestation using multivariable logistic regression analysis with backward stepwise elimination to determine which of the factors among maternal characteristics and medical and obstetric history had a significant contribution in predicting SGA <10th.[12] Fetal growth velocity was defined as the difference in EFW Z-scores or AC Z-scores between the third and second trimester scans divided by the time interval in days between them. Univariable and multivariable regression analysis was carried out to determine whether the addition of maternal factors and EFW or AC growth velocity to the EFW Z-score at 35^{+0} - 36^{+6} weeks' gestation improved the performance of screening for SGA neonates <10th and <3rd percentile delivering within two weeks and at any stage after assessment. The performance of screening was determined by receiver operating characteristic (ROC) curves. We estimated detection rates (95% confidence intervals [CI]) for fixed screen positive rate of 10% and screen positive rates (95% CI) for fixed detection rates of 85%, 90% and 95%.

The statistical software package SPSS 24.0 (IBM SPSS Statistics for Windows, Version 24.0, Armonk, NY: IBM Corp; 2016) and Medcalc (Medcalc Software, Mariakerke, Belgium) were used for data analyses.

RESULTS

Patient characteristics

The characteristics of the study population are shown in Table 1. In the group with SGA neonates, compared to those with birthweight ≥10th percentile, the median maternal age, weight and height, EFW Z-score and AC Z-score at both visits and birthweight z-score were lower, more women were of non-White racial origin, were smokers, had chronic hypertension, were nulliparous or parous with previous affected pregnancy by SGA, and less women had diabetes mellitus type 1.

Prediction of SGA neonates from EFW at 35^{+0} - 36^{+6} weeks' gestation

Receiver operating characteristics curves for prediction by EFW at 35^{+0} - 36^{+6} weeks' gestation of SGA neonates <10th and <3rd percentiles born within two weeks and at any time from assessment are shown in Figure 1. The group with EFW Z-score <-1.2106, which is equivalent to 10% of the population the 10th percentile, contained 63.4% (95% CI 62.0, 64.7) of neonates with birthweight <10th percentile and 74.2% (95% CI 72.2, 76.1) of neonates with birthweight <3rd percentile born at any stage after screening. The respective values for SGA neonates born within two weeks of screening were 76.8% (95% CI 74.4, 79.0) and 81.3% (95% CI 78.2, 84.0). In the group of fetuses with EFW <10th percentile, 43.7% were born with birthweight ≥10th percentile. For a desired 90% detection rate of SGA neonates delivering at any stage after assessment the necessary screen positive rate would be 33.7% for SGA <10th percentile and 24.4% for SGA <3rd percentile.

Prediction of SGA neonates: additional contribution of maternal risk factors and growth velocity

Multivariable logistic regression analysis demonstrated that in the prediction of SGA neonates with birthweight <10th and <3rd percentiles there was a significant contribution from maternal risk factors, EFW Z-score at 35^{+0} - 36^{+6} weeks' gestation and AC growth velocity, but not EFW growth velocity (Table 2).

The AUROC for SGA neonates <10th percentile born within two weeks from assessment in screening by maternal risk factors and EFW Z-score (0.936, 95% CI 0.929, 0.943) was marginally higher than that of screening by EFW Z-score alone (0.933, 95% CI 0.926, 0.941; p=0.040); the AUROC in screening by maternal risk factors and EFW Z-score was not improved by addition of AC growth velocity (p=0.232). In prediction of SGA neonates <3rd percentile, addition of maternal risk factors did not improve the performance of screening that was achieved by EFW Z-score alone (p=148) and addition of AC growth velocity did not improve the performance of screening that was achieved by a combination of maternal risk factors and EFW Z-score (p=0.058) (Table 3).

The AUROC for SGA neonates <10th percentile born at any time from assessment in screening by a combination of maternal risk factors and EFW Z-score at 35^{+0} - 36^{+6} weeks (0.895, 95% CI 0.890, 0.899) was significantly higher than that of screening by EFW Z-score alone (0.883, 95% CI 0.879, 0.888 p<0.0001); this was also the case for SGA neonates <3rd percentile (0.924, 95% CI 0.919, 0.930 vs. 0.918, 95% CI 0.912, 0.923; p<0.001) (Table 3). Addition of AC growth velocity did not improve the performance of screening that was achieved by a combination of maternal

risk factors and EFW Z-score, for prediction of either SGA neonates <10th percentile (p=0.103) or <3rd percentile (p=0.061) (Table 3).

The detection rate, at 10% screen positive rate, of SGA neonates <10th percentile born within two weeks from assessment, in screening by EFW alone (76.8%) was marginally improved by the addition of maternal risk factors (78.6%), but addition of AC growth velocity (78.6%) did not improve the detection rate that was achieved by a combination of maternal risk factors and EFW Z-score. In the case of SGA neonates <3rd percentile the detection rate in screening by EFW alone (81.7%) was not improved by the addition of maternal risk factors (81.7%) or the addition of maternal risk factors and AC growth velocity (82.1%) (Table 3). The detection rate, at 10% screen positive rate, of SGA neonates <10th percentile born at any stage after assessment, in screening by EFW alone (63.4%) was significantly improved by the addition of maternal risk factors (67.1%), but addition AC growth velocity (67.1%) did not improve the detection rate achieved by a combination of maternal risk factors and EFW (Table 3). In the case of SGA neonates <3rd percentile the detection rate, at 10% screen positive rate, in screening by EFW alone (74.2%) was marginally improved by the addition of maternal risk factors (75.9%), and addition AC growth velocity (76.4%) did not improve the detection rate achieved by a combination of maternal risk factors and EFW (Table 3).

The screen positive rates necessary to achieve prediction of 85%, 90% and 95% of SGA neonates delivering within two weeks and at any stage from assessment are shown in Table 4. If the desired detection rate of SGA neonates <10th percentile born within two weeks from assessment was 90%, the necessary screen positive rate in screening by maternal risk factors and EFW was not significantly different from that of screening by EFW alone (20.7% vs 21.3%); this was also the case for SGA neonates <3rd percentile (16.0% vs. 17.2%). However, for SGA neonates <10th percentile born at any stage from assessment the necessary screen positive rate for 90% detection rate in screening by maternal risk factors and EFW was lower than that of screening by EFW alone (31.0% vs 33.7%; p<0.001); this was also the case for SGA neonates <3rd percentile (20.8% vs. 24.4%; p<0.001).

DISCUSSION

Main findings of the study

The findings of this study demonstrate the performance of screening for SGA neonates by routine ultrasound examination at 35+0 - 36+6 weeks' gestation. Screening by EFW, at 10% screen positive rate, at EFW cut-off of the 10th percentile predicted 63% of neonates with birthweight <10th percentile and 74% of those with birthweight <3rd percentile born at any stage after screening; 44% of fetuses thought to be SGA were born with birthweight ≥10th percentile. The performance of EFW <10th percentile was better for babies born within two weeks of assessment with prediction of 77% of neonates with birthweight <10th percentile and 81% of those with birthweight <3rd percentile. To accomplish a detection rate of 90% for SGA neonates at the 35+0 - 36+6 weeks' scan we would need to classify about 35% of the population as being screen positive need to utilize the EFW cut-off at the 35th percentile.
Prediction of 90% of SGA neonates necessitates

The predictive performance for SGA neonates of EFW at 35+0 - 36+6 weeks' gestation was improved by addition of maternal demographic characteristics and medical history; addition of maternal risk factors improved the prediction of SGA neonates with birthweight <10th percentile born at any stage after screening from 63% to 67%. We have previously reported that the risk of delivering SGA neonates increases with maternal age, decreases with maternal weight and

height, it is higher in women of Black, South Asian, East Asian and mixed racial origins than in White women, in cigarette smokers, in those with chronic hypertension, diabetes mellitus type II and in parous women with prior history of SGA. The risk is lower in parous women without prior history of SGA and in those with diabetes mellitus type I.[12]

The predictive performance for SGA neonates of EFW at 35^{+0} - 36^{+6} weeks' gestation was not improved by addition of fetal growth velocity between 19^{+0} - 23^{+6} and 35^{+0} - 36^{+6} weeks' gestation.

Comparison with findings from previous studies

Our findings that EFW <10th percentile predicts 63% and 74% of neonates with birthweight <10th and <3rd percentile, respectively, are consistent with the results of previous late third-trimester studies. Fadigas *et al*, examined 5,515 pregnancies at 35-37 weeks and reported that EFW <10th percentile predicted 63% and 73% of neonates with birthweight <10th and <3rd percentile, respectively.[8] Triunfo *et al*, examined 946 pregnancies at 36-38 weeks and reported that EFW <10th percentile predicted 59% and 83% of neonates with birthweight <10th and <3rd percentile, respectively.[18] Souka *et al*, examined 2,288 pregnancies at 34-37 weeks and reported that EFW <10th percentile predicted 75% of neonates with birthweight <5th percentile.[7]

Our findings that the prediction of SGA neonates provided by EFW is improved by the addition of maternal risk factors (63% to 67% for SGA <10th percentile) are consistent with the results of Fadigas *et al*, who reported that addition of maternal factors improved the prediction of SGA neonates from 63% to 66%.[8]

We found that growth velocity between the second and third trimesters did not improve the prediction of SGA neonates provided by EFW at 35^{+0} - 36^{+6} weeks' gestation. Studies examining fetal growth velocity and conditional fetal growth percentiles, which are calculated taking into account an EFW earlier in pregnancy, compared with conventional weight-for-gestational-age charts, have reported contradictory results in the prediction of adverse perinatal outcomes.[11,19-22] However, the objective of our study was to predict SGA neonates rather than adverse perinatal outcome. Our results are consistent with those of two previous studies that examined 3,440 and 2,696 pregnancies, respectively,[23,24] and reported that growth velocity, conditional growth percentiles or serial fetal biometry did not improve the prediction of SGA neonates provided by the last EFW alone.

Implications for clinical practice

In the proposed new pyramid of pregnancy care,[25] an integrated clinic 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 preterm PE and / or SGA and through pharmacological intervention to reduce the prevalence of these complications.[26-29] The objective of subsequent visits, at around 20 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 have previously proposed that assessment at 20 weeks' gestation would stratify the population into a high-risk group, which would comprise of <0.5% of all pregnancies and contain all cases of SGA delivering <32 weeks, a moderate-risk group comprising of about 15% of pregnancies and containing about 90% of cases of SGA that deliver at 32-36 weeks and a low-risk group that would contain all cases of SGA that deliver at term.[30] The high-risk group would require reassessment at 26-30 weeks and again at 32 and 36 weeks if not delivered, the moderate-risk group would be reassessed at 32 and 36 weeks and the low-risk group would be reassessed at 36 weeks.

This study provides the necessary data for development of policies to achieve prenatal prediction of a desired percentage of SGA neonates near term. We have shown that the prediction of SGA neonates achieved by EFW can be improved by maternal factors but not by growth velocity. In a previous study we have reported that the prediction by EFW and maternal factors can be improved marginally by the addition of biomarkers of impaired placentation, including serum placental growth factor and uterine artery and fetal middle cerebral artery pulsatility index.[12]

Strengths and limitations of the study

The strengths of this screening study for SGA neonates are first, examination of a large population of pregnant women attending for routine assessment of fetal growth and wellbeing at both 19^{+0} - 23^{+6} and 35^{+0} - 36^{+6} weeks' gestation, second, trained sonographers that carried out fetal biometry according to a standardized protocol and use of a widely used model for calculation of EFW [14] which has been shown to be the most accurate one among 70 previously reported models,[13] third, use of the Fetal Medicine Foundation fetal and neonatal references ranges which have a common median.[15]

A potential limitation of the study is the long interval between the two ultrasound examinations that defined growth velocity and the proximity of the second scan to delivery which would inevitably minimize the contribution of growth velocity to that of EFW at 35-37 weeks. This was the consequence of the design of our study which relied on data obtained from two routine ultrasound examinations in pregnancy. The extent to which a shorter interval between the two scans improves the contribution of growth velocity to the prediction of SGA remains to be determined. The second potential limitation of the study is the use of growth velocity rather than more complex methods of evaluating longitudinal growth; however, there is no evidence of superiority of the latter over the former.[24,31-33]

Conclusions

The performance of sonographic EFW for prediction of SGA neonates is highest if the interval between assessment and birth is short. Since 85% of SGA neonates are born at ≥37 weeks' gestation a routine third trimester scan is best performed at 36 than at 32 weeks' gestation. The performance of screening by EFW at 35^{+0} - 36^{+6} weeks is improved by maternal demographic characteristics and medical history but not by growth velocity between the second and third trimesters. Our results suggest, that to accomplish a detection rate of 90% for SGA neonates at the 35^{+0} - 36^{+6} weeks' scan we would need to classify about 35% of the population as being screen positive will need to utilize the EFW cut-off at the 35th percentile. Future studies will investigate whether growth velocity improves the performance of the 35^{+0} - 36^{+6} weeks' scan in the prediction of adverse perinatal outcome.

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FIGURE LEGENDS

Figure 1. Receiver operating characteristics curves of maternal factors (black line), estimated fetal weight at 35^{+0} - 36^{+6} weeks' gestation (blue), abdominal circumference growth velocity (green), and combination of the three (red), in the prediction of small for gestational age neonates with birth weight below the 10th percentile delivering within two weeks (left) and at any time (right) from assessment.

Figure 2. Receiver operating characteristics curves of maternal factors (black line), estimated fetal weight at 35^{+0} - 36^{+6} weeks' gestation (blue), abdominal circumference growth velocity (green), and combination of the three (red), in the prediction of small for gestational age neonates with birth weight below the 3rd percentile delivering within two weeks (left) and at any time (right) from assessment.

Table 1- Maternal and pregnancy characteristics in pregnancies delivering small for gestational age neonates <10th percentile and those without

Characteristic	Non-SGA (n=38,994)	SGA<10th percentile (n=5,049)	P-value
Maternal age in years, median (IQR)	31.7 (27.5, 35.4)	30.9 (26.2, 35.0)	<0.001
Maternal weight in Kg, median (IQR)	80.0 (71.5, 91.0)	73.4 (65.5, 83.4)	<0.001
Maternal height in cm, median (IQR)	165 (161, 170)	163 (158, 167)	<0.001
Racial origin			
White, n (%)	29,825 (76.5)	3,224 (63.9)	<0.001
Black, n (%)	5,684 (14.6)	1,055 (20.9)	<0.001
South Asian, n (%)	1,594 (4.1)	467 (9.2)	<0.001
East Asian, n (%)	761 (2.0)	121 (2.4)	0.034
Mixed, n (%)	1,130 (2.9)	182 (3.6)	0.005
Cigarette smoker, n (%)	2,832 (7.3)	726 (14.4)	<0.001
Conception			
Natural, n (%)	37,645 (96.5)	4,851 (96.1)	
Ovulation drugs, n (%)	219 (0.6)	34 (0.7)	0.323
In vitro fertilization, n (%)	1,130 (2.9)	164 (3.2)	0.165
Medical conditions			
Chronic hypertension, n (%)	459 (1.2)	88 (1.7)	0.001
Diabetes mellitus type 1, n (%)	156 (0.4)	5 (0.1)	0.001
Diabetes mellitus type 2, n (%)	178 (0.5)	18 (0.4)	0.315
Past obstetric history			
Nulliparous, n (%)	17,114 (43.9)	2,811 (55.7)	<0.001
Parous with prior SGA, n (%)	2,989 (7.7)	920 (18.2)	<0.001
Parous without prior SGA, n (%)	18,891 (48.4)	1,318 (26.1)	<0.001
GA at screening at $19^{+0} - 23^{+6}$ weeks, median (IQR)	21.7 (21.1, 22.1)	21.7 (21.1, 22.1)	0.003
EFW Z-score at $19^{+0} - 23^{+6}$ weeks, median (IQR)	0.06 (-0.58, 0.69)	-0.56 (-1.17, 0.07)	<0.001
AC Z-score at $19^{+0} - 23^{+6}$ weeks, median (IQR)	-0.01 (-0.29, 0.28)	-0.24 (-0.52, 0.04)	<0.001
GA at screening at $35^{+0}-36^{+6}$ weeks, median (IQR)	36.1 (35.9, 36.4)	36.1 (35.9, 36.4)	0.003
EFW Z-score at $35^{+0}-36^{+6}$ weeks, median (IQR)	0.20 (-0.39, 0.81)	-1.20 (-1.88, -0.65)	<0.001
AC Z-score at $35^{+0}-36^{+6}$ weeks , median (IQR)	0.00 (-0.47, 0.49)	-1.01 (-1.49, -0.57)	<0.001
GA at delivery in weeks, median (IQR)	40.0 (39.0, 40.9)	39.4 (38.2, 40.3)	<0.001
Birthweight Z-score, median (IQR)	0.13 (-0.45, 0.75)	-1.72 (-2.14, -1.48)	<0.001
Birthweight in grams, median (IQR)	3490 (3220, 3790)	2715 (2510, 2860)	<0.001

GA = gestational age; EFW = estimated fetal weight; IQR = interquartile range; SGA = small for gestational age; PE = preeclampsia.

Table 2. Multivariable logistic regression analysis in prediction of small for gestational age neonates <10th and <3rd percentiles from maternal and pregnancy characteristics, estimated fetal weight Z-score at 35^{+0} - 36^{+6} weeks' gestation, estimated fetal weight growth velocity and abdominal circumference growth velocity.

Characteristic	Univariable		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Birthweight <10th percentile				
Maternal factors	17.98 (16.01-20.21)	<0.001	6.82 (5.94-7.82)	<0.001
Estimated fetal weight Z-score	0.15 (0.14-0.16)	<0.001	0.18 (0.16-0.19)	<0.001
Estimated fetal weight growth velocity	$8.12e^{-41}$ ($3.16e^{-42}$-$2.08e^{-39}$)	<0.001	-	-
Abdominal circumference growth velocity	$8.46e^{-80}$ ($4.36e^{-82}$-$1.64e^{-77}$)	<0.001	$2.10e^{-04}$ ($7.50e^{-08}$-0.584)	0.036
Birthweight <3rd percentile				
Maternal factors	21.59 (18.07-25.08)	<0.001	5.42 (4.41-6.67)	<0.001
Estimated fetal weight z-score	0.15 (0.14-0.16)	<0.001	0.18 (0.17-0.20)	<0.001
Estimated fetal weight growth velocity	$9.18e^{-50}$ ($7.75e^{-52}$-$1.09e^{-47}$)	<0.001	-	-
Abdominal circumference growth velocity	$2.17e^{-91}$ ($1.06e^{-94}$-$4.45e^{-88}$)	<0.001	$4.47e^{-09}$ ($3.71e^{-14}$-0.001)	0.001

OR = odds ratio; CI = confidence interval; SGA = small for gestational age

Table 3. Performance of prediction of small for gestational age neonates with birth weight <10th, and <3rd percentile delivering within two weeks and at any stage after screening at $35^{+0} – 36^{+6}$ weeks' gestation.

Screening test	SGA <10th percentile		SGA < 3rd percentile	
	AUROC curve (95% CI)	DR at 10% SPR % (95% CI)	AUROC curve (95% CI)	DR at 10% SPR % (95% CI)
SGA within 2 weeks				
EFW Z-score at 35^{+0} - 36^{+6} weeks	0.933 (0.926, 0.941)	76.8 (74.4, 79.0)	0.945 (0.937, 0.952)	81.3 (78.2, 84.0)
Maternal factors	0.693 (0.675, 0.710)	30.3 (27.7, 32.5)	0.695 (0.673, 0.717)	30.3 (27.1, 33.8)
EFW growth velocity	0.828 (0.815, 0.842)	55.4 (53.6, 57.1)	0.856 (0.840, 0.871)	57.9 (54.4, 60.7)
AC growth velocity	0.884 (0.873, 0.895)	64.3 (62.0, 66.7)	0.900 (0.888, 0.913)	70.9 (67.1, 73.4)
EFW Z-score + Maternal factors	0.936 (0.929, 0.943)	78.6 (76.1, 80.7)	0.946 (0.939, 0.954)	81.7 (78.7, 84.5)
EFW Z-score + AC growth velocity + Maternal factors	0.936 (0.929, 0.944)	78.6 (76.1, 80.7)	0.947 (0.940, 0.954)	82.1 (79.1, 84.9)
SGA at any stage				
EFW Z-score at 35^{+0} - 36^{+6} weeks	0.883 (0.879, 0.888)	63.4 (62.0, 64.7)	0.918 (0.912, 0.923)	74.2 (72.2, 76.1)
Maternal factors	0.713 (0.706, 0.721)	31.6 (30.0, 32.6)	0.726 (0.715, 0.738)	33.9 (31.7, 35.9)
EFW growth velocity	0.737 (0.730, 0.744)	36.7 (34.2, 38.5)	0.793 (0.782, 0.803)	47.5 (45.2, 49.7)
AC growth velocity	0.808 (0.802, 0.814)	47.0 (45.1, 49.4)	0.855 (0.847, 0.864)	58.4 (56.1, 60.7)
EFW Z-score + Maternal factors	0.895 (0.890, 0.899)	67.1 (65.9, 68.4)	0.924 (0.919, 0.930)	75.9 (74.0, 77.8)
EFW Z-score + AC growth velocity + Maternal factors	0.895 (0.890, 0.899)	67.1 (65.9, 68.4)	0.925 (0.919, 0.930)	76.4 (74.5, 78.3)

AUROC = area under the receiver operating characteristic curves; CI = confidence interval; EFW = estimated fetal weight; AC = abdominal circumference; SGA = small for gestational age; DR = detection rate; SPR = screen positive rate

Table 4. Screen positive rate necessary to achieve prediction of 85%, 90% and 95% of small for gestational age neonates delivering within two weeks and at any stage after assessment at $35^{+0} - 36^{+6}$ weeks' gestation.

Screening test	SPR for 85% DR % (95% CI)	SPR for 90% DR% (95% CI)	SPR for 95% DR% (95% CI)
SGA within 2 weeks			
SGA <10th percentile			
EFW Z-score at 35^{+0} - 36^{+6} weeks	16.0 (14.9, 17.2)	21.3 (20.0, 22.6)	31.2 (29.7, 32.6)
EFW Z-score + Maternal factors	14.6 (13.5, 15.7)	20.7 (19.4, 22.0)	30.8 (29.3, 32.2)
EFW Z-score + Maternal factors + AC growth velocity	14.4 (13.3, 15.5)	20.6 (19.3, 21.9)	30.5 (29.0, 31.9)
SGA <3rd percentile			
EFW Z-score at 35^{+0} - 36^{+6} weeks	12.5 (11.5, 13.5)	17.2 (16.1, 18.4)	24.0 (22.8, 25.3)
EFW Z-score + Maternal factors	11.6 (10.7, 12.6)	16.0 (14.9, 17.1)	22.3 (21.1, 23.5)
EFW Z-score + Maternal factors + AC growth velocity	11.4 (10.5, 12.4)	15.9 (14.8, 17.0)	21.2 (20.0, 22.5)
SGA at any stage			
SGA <10th percentile			
EFW Z-score at 35^{+0} - 36^{+6} weeks	26.3 (26.0, 27.1)	33.7 (33.2, 34.2)	46.3 (45.8, 46.8)
EFW Z-score + Maternal factors	23.3 (22.8, 23.7)	31.0 (30.6, 31.5)	42.0 (41.5, 42.4)
EFW Z-score + Maternal factors + AC growth velocity	23.0 (22.6, 23.4)	31.1 (30.7, 31.6)	41.8 (41.3, 42.5)
SGA <3rd percentile			
EFW Z-score at 35^{+0} - 36^{+6} weeks	17.7 (17.3, 18.0)	24.4 (24.1, 24.9)	35.4 (34.9, 35.8)
EFW Z-score + Maternal factors	15.9 (15.6, 16.3)	20.8 (20.5, 21.0)	31.8 (31.4, 32.2)
EFW Z-score + Maternal factors + AC growth velocity	15.8 (15.5, 16.2)	21.6 (21.2, 22.0)	32.5 (32.0, 32.9)

SPR = screen positive rate; CI = confidence interval; SGA = small for gestational age; EFW = estimated fetal weight; AC = abdominal circumference; DR = detection rate.