
Paediatric and Perinatal Epidemiology

46 doi: 10.1111/ppe.12251

Does the Presence of Risk Factors for Fetal Growth Restriction Increase the Probability of Antenatal Detection? A French National Study

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Abstract

Background: Screening for fetal growth restriction (FGR) is a major component of prenatal care. We investigated whether the presence of maternal and pregnancy risk factors for FGR improves the antenatal suspicion of FGR for infants born small-for-gestational age (SGA) as well as their impact on screening specificity.

Methods: Data are from a representative sample of births from the 2010 French National Perinatal Survey ($n = 14\,100$). Detection of FGR was determined by a suspicion of FGR noted in medical charts. Analyses were performed for singleton infants with birthweight under the 10th percentile (SGA), under the 3rd percentile (severely SGA), and above the 10th percentile (false positives) of French references. We studied risk factors for FGR (medical and obstetric conditions, advanced maternal age, nulliparity, body mass index and smoking) using multivariable Poisson regression to derive adjusted risk ratios (aRR).

Results: Of SGA infants, 21.7% were suspected of FGR. The presence of obstetric and medical risk factors for FGR was associated with higher suspicion among SGA infants [RR 2.1, 95% confidence interval (CI) 1.7, 2.7]. However, despite the presence of these factors, 60% and 40% of SGA and severely SGA infants, respectively, were not suspected of FGR. Two per cent of normal birthweight infants were suspected of FGR, increasing to 5% when obstetric and medical risk factors were present. Smoking and older maternal age were unrelated to suspicion while females were more likely to be suspected of FGR.

Conclusion: Our results suggest that better risk assessment could improve antenatal identification of FGR. Sex-specific fetal growth references should be used to avoid systematic bias linked to sex.

Keywords: *fetal growth restriction, small-for-gestational age, antenatal detection, risk factors, false positives.*

Fetal growth restriction (FGR) is associated with an increased risk of stillbirth, neonatal death and short- and long-term morbidity.[1,2] In order to avoid these adverse outcomes, the management of pregnancies with FGR involves close monitoring of fetal well-being and early delivery when necessary. Screening for FGR during pregnancy is thus a central component of prenatal care, as highlighted in recent national guidelines from the United States, United Kingdom, France, New Zealand, and Canada.[3–7] First-line tools include risk factor assessment at the beginning and during pregnancy, and the measurement of symphysis fundal height to identify women requiring closer surveillance of fetal growth. Ultrasound assessments of fetal growth are carried out routinely in some countries or solely for women at higher risk in others. All recommendations advocate identification and surveillance of fetuses with an estimated fetal weight (or other biometric parameters) under the 10th percentile of growth references in order to differentiate between constitutionally small, but normal, fetuses and those with growth faltering.[4–6]

Despite the consensus on FGR screening during pregnancy, the few large-scale studies assessing its effectiveness have reported low detection rates: 10–36% of babies born small-for-gestational (SGA),

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defined as a birthweight below the 10th percentile.[8–13] We recently confirmed these findings in a French national study where only 21% of SGA infants were suspected of FGR during pregnancy.[14] Reasons for low detection rates may be poor effectiveness of fundal height assessment and ultrasound to detect SGA infants,[15,16] the timing of routine ultrasounds,[17,18] and the absence of longitudinal growth assessments growth.[19] Inadequate use of risk factors to identify pregnancies at risk of FGR may also play a role. All professional guidelines recommend closer surveillance of women with risk factors for FGR including obstetric history of SGA, hypertensive disorders, advanced maternal age, smoking, nulliparity, and low and high body mass index (BMI).[3–6]

As poor risk factor assessment may be particularly amenable to provider training, we investigated if the presence of known risk factors for FGR was associated with the suspicion of FGR among SGA infants. Analyses were also carried out among normal birthweight infants suspected with FGR during pregnancy to explore how the presence of risk factors affected the specificity of screening.

Methods

Study population

Our data were abstracted from a population-based study from the 2010 French National Perinatal Survey, which aimed to monitor key indicators of perinatal health and care in France. This survey includes all births (live and stillbirths) at or after 22 weeks of gestation or newborns with a birthweight of at least 500 grams in all maternity units over a one-week period of March 2010 ($n = 15\ 418$).[20] Data on maternal sociodemographic characteristics, antenatal care and health behavior were obtained from interwiews with women after delivery while data on obstetric care and medical conditions were abstracted from medical charts.

Comparisons for several perinatal indicators (e.g. maternal age, gestational age) available in birth certificate statistics and hospital discharge statistics show that the sample is representative of all births in 2010.[20,21] The National Council on Statistical Information (Comité du Label) and the French Commission on Information Technology and Liberties (CNIL) approved this survey (registration number 909003).

In our study, births outside of continental France ($n = 515$), multiple pregnancies ($n = 443$), and births with missing data on gestational age at birth, birthweight, and fetal sex ($n = 304$) were excluded. Medical terminations of pregnancy ($n = 53$) were also excluded, leading to the exclusion of severe congenital anomalies. Live infants with congenital anomalies were retained in the sample after review of these cases found that the anomalies were minor. These cases represented 1.7% or our sample. The final study population consisted of 14 100 infants.

Variables

Antenatal suspicion of FGR was defined as the suspicion of poor fetal growth as noted in the medical charts. This information was abstracted by midwives from medical charts after delivery and during the hospital stay. According to French recommendations,[22,23] an ultrasound should be performed for each trimester of pregnancy, including a third trimester ultrasound between 30 and 35 weeks of gestation. Its main objective is to detect abnormalities of fetal growth and congenital anomalies which cannot be diagnosed earlier. Quality standards have been developed by the French College of fetal ultrasound.[5] Suspicion of FGR is usually based on an estimated fetal weight or other biometric measurements under the 10th percentile for-gestational age and additional ultrasounds are performed every 3 weeks with Doppler measurements.[5] Further details were not noted on ultrasounds or Doppler velocimetry.

Our independent variables included clinical and sociodemographic factors known to be associated with increased risk of FGR. Maternal characteristics were medical and obstetric risk factors, age, parity, pre-pregnancy BMI and smoking during the third trimester of pregnancy. It is difficult to differentiate between the physiological and pathological effects of parity on fetal growth, but as reported in other studies,[24,25] as well as in professional guidelines on FGR in France and the UK, nulliparity is considered as a risk factor for growth restriction and therefore was included in the study.[4,5] We also included BMI because low BMI, as well as high BMI, are known to be related to fetal growth.[26] Information was not available on pregnancy intervals in the French national survey.

We developed a classification for medical and obstetric factors into three levels of clinical risk using

French National Health Board recommendations.[22,23] These factors, included medical and obstetric history as well as complications of the current pregnancy, abstracted from notes recorded by the team in medical records. The aim of this three-tiered classification was to test if the presence of medical and obstetric risk factors for FGR increased antenatal suspicion. We thus distinguished (1) medical and obstetric risk factors known to impact on poor fetal growth (previous pre-eclampsia, stillbirth or SGA infant, chronic hypertension and/or for the current pregnancy, including gestational hypertension, pre-eclampsia and fetal congenital anomalies) from (2) other medical and obstetric complications unrelated to FGR (previous pregnancy complications, diseases requiring visits to a doctor, complications of the current pregnancy). A third group included pregnancies with none of the above factors and was considered to be low-risk (Table S1).

We also included fetal sex in our models. While birthweight percentiles are adjusted for fetal sex, ultrasound references used to detect FGR are not.[27] Further, fetal sex may be associated with some of the complications leading to FGR, such as hypertensive diseases of pregnancy.[28] So, although fetal sex is a biological growth parameter and not a risk factor for poor growth, it could impact on suspicion rates.

Birthweight was expressed in classes of birthweight percentile for-gestational age and sex using French reference standards.[29] We also expressed birthweight as a continuous variable using the birthweight ratio which takes into consideration gestational age and sex (birthweight/mean birthweight by gestational age and sex).[30] SGA was defined as a birthweight under the 10th percentile. Severe SGA has been defined in the literature using several definitions (<3rd percentile, <5th percentile, <-2 standard deviations).[1,31] We chose the 3rd percentile because this corresponds to the threshold most often used in France as shown by recent recommendations.[5] Fetal growth curves customized on maternal characteristics are not used in France.[5]

Statistical analysis

We first described the proportions of infants suspected of FGR by birthweight percentile and presence of medical or obstetric risk factors. We then estimated the percent of infants suspected of FGR by selected risk factors for infants born with birthweights below the 10th and the 3rd percentile. We carried out similar analyses for infants with birthweights over the 10th percentile separately in order to estimate the specificity of suspicion in the presence of those risk factors. Chi-squared tests were used for comparison of categorical variables. We used multivariable Poisson regressions to estimate risk ratios, with their 95% confidence intervals (CIs), adjusted on clinical and sociodemographic risk factors known to impact on fetal growth and on obstetric decisions to increase surveillance.[32–34] These risk factors were medical and obstetric factors, maternal age, parity, BMI, smoking in the third trimester of pregnancy and fetal sex. Models were also adjusted for the birthweight ratio, as our aim was to measure the independent effects of specific risk factors on suspicion of FGR for a given weight.

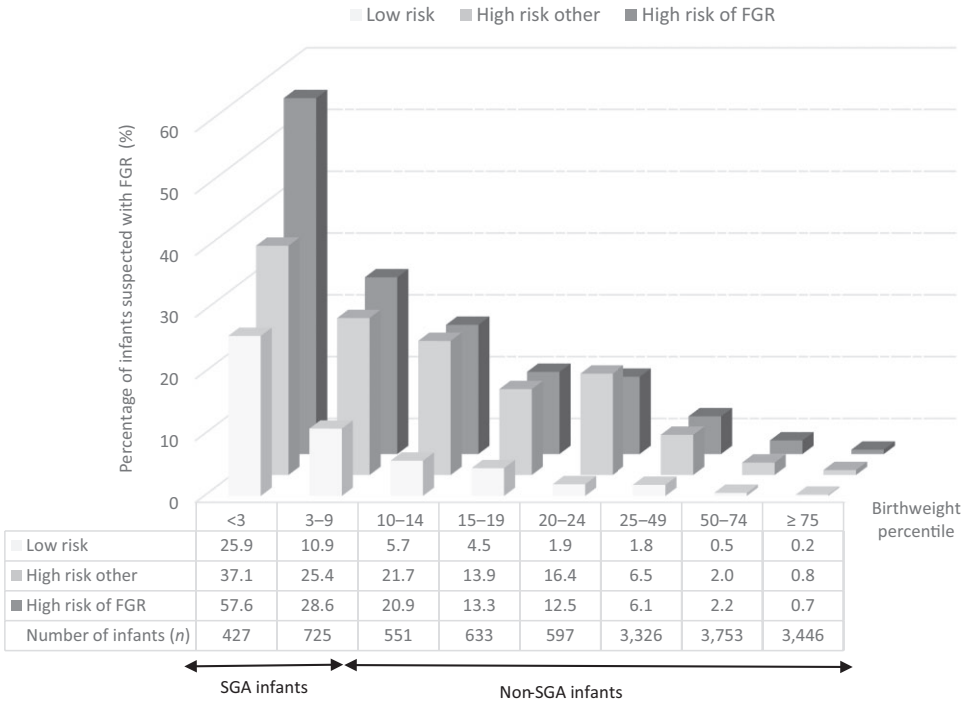
In order to confirm that socio-economic factors did not influence our results, we also ran our models including two socio-economic risk factors (low educational level and inadequate prenatal care), which may be on the pathway between other clinical risk factor and poor detection. Inadequate prenatal care was defined as a number of prenatal visits and/or ultrasounds below the recommended number given the gestational age at delivery and/or initiation of care after the first trimester of pregnancy based on French recommendations.[22]

Missing data

Most variables had low proportions of missing data (<5% for maternal age and parity). BMI and smoking had the largest number of missing observations, but did not exceed 10% of our sample. However, given the number of variables included in our analysis, listwise deletion of missing cases led to exclusion of about 15% of our sample. We therefore used multiple imputations with chained equations with linear regression for continuous variables, logistic regression for categorical variables and ordered logistic regression for ordinal variables to generate values for missing data.[35] For each of the three models, the number of imputations was similar to the percentage of observations that were missing (m = 18). The analyses were performed using STATA 13.0 software (StataCorp LP, College Station, TX, USA).

Results

Figure 1 shows the rates of suspicion of FGR by birthweight percentile and presence of medical or



	<3	3–9	10–14	15–19	20–24	25–49	50–74	≥ 75
Low risk	25.9	10.9	5.7	4.5	1.9	1.8	0.5	0.2
High risk other	37.1	25.4	21.7	13.9	16.4	6.5	2.0	0.8
High risk of FGR	57.6	28.6	20.9	13.3	12.5	6.1	2.2	0.7
Number of infants (*n*)	427	725	551	633	597	3,326	3,753	3,446

Figure 1. Antenatal suspicion of fetal growth restriction (FGR) by birthweight percentile and clinical risk status.

obstetric risk factors. Rates of suspicion of FGR decreased with increasing birthweight percentile and remained higher across the birthweight spectrum for pregnancies associated with medical or obstetric risk factors for FGR as well as those with other complications. For instance, among pregnancies with medical or obstetric risk factors for FGR, rates of suspicion were of 57.6% and 28.6% for infants with birthweights below the 3rd and between the 3rd and 9th percentiles, respectively. For pregnancies with medical or obstetric risk factors unrelated to FGR, the suspicion rates were 37.1% and 25.4%, respectively.

In Table 1, we display maternal and neonatal characteristics for the entire sample. Most women were between 20 and 34 years old and 17% of smoked during the third trimester of pregnancy. Low-risk pregnancies constituted 75% of the total and women had an average of five ultrasounds during pregnancy. In our sample, 8.9% of infants had a birthweight below the 10th percentile and 3.2% below the 3rd percentile.

Table 2 describes the antenatal suspicion of FGR by presence of risk factors for SGA infants with a birthweight below the 10th and the 3rd percentiles. Overall, 21.7% and 33.0% of infants with a birthweight less than the 10th and the 3rd percentiles, respectively, were suspected of having FGR during pregnancy. Fetal sex was the only factor associated with a suspicion of FGR among SGA infants with a birthweight under the 10th percentile. Females were more often suspected of FGR than males: 25.1% vs. 18.4% ($P = 0.005$) and this remained significant after adjustment [aRR 1.4 (95% CI 1.1, 1.8)]. Well-known risk factors for FGR were not linked to a higher probability of suspicion including smoking more than 10 cigarettes a day during the third trimester and maternal age over 40. For infants with severe SGA, only the presence of medical and obstetric risk factors for FGR was related to suspicion [aRR 1.9 (95% CI 1.4, 2.6)].

Table 3 presents clinical and sociodemographic factors related to the suspicion of FGR during pregnancy for infants with a birthweight over the 10th percentile (false positives). Two per cent ($n = 271$) of the 12 881 infants with a normal birthweight were suspected of FGR. Many variables were associated with a suspicion of FGR in unadjusted analyses: younger women, low BMI and smoking during the third trimester of pregnancy. However, after controlling for the birthweight ratio and other factors, a higher probability of suspicion was associated with medical and obstetric risk factors, fetal sex and low BMI (<18.5 kg/m^2). In contrast, maternal age between 35

Table 1. Maternal and neonatal characteristics in the entire sample

	All infants Percentage or mean (SD)
Total (*n*)	14 100
Maternal characteristics	
Maternal age (years)	
≤19	2.4
20–34	78.5
35–39	15.6
40 +	3.5
Parity	
Nulliparous	43.4
Multiparous	56.6
Body mass index (kg/m^2)	
<18.5	8.3
18.5–24.9	64.5
25–29.9	17.3
≥30	9.9
Smoke in third trimester	
No	83.0
1–9 cigarettes/day	12.2
+10 cigarettes/day	4.8
Medical/obstetrical factors[a]	
Risk factors for FGR	11.7
Other risk factors	13.0
No risk factor (low risk)	75.3
Number of ultrasounds	4.9 (0.1)
Inadequate prenatal care	13.1
Neonatal characteristics	
Male sex	52.5
Birthweight percentile	
<3rd	3.2
3rd–9th	5.5
10th–24th	13.2
≥25th	78.1
Birthweight ratio	1.0 (0.0)

[a]Pregnancies with risk factors for fetal growth restriction (FGR) were those with medical and obstetric risk factors known to impact on fetal growth (previous hypertension, stillbirth or small-for-gestational (SGA) infant and for the current pregnancy, gestational hypertension, pre-eclampsia, and congenital anomalies); Pregnancies with other risk factors were those with all other medical and obstetric risk factors (diseases requiring regular visits to a doctor, complications of the current pregnancy); low-risk pregnancies were all other pregnancies.

and 39 years old was associated with a lower probability of suspicion. About 5% of women with medical and obstetric risk factors were suspected of having a growth restricted fetus. In low-risk women, this percentage was 1.3%.

Analyses including socio-economic factors (Tables S2 and S3) and those using multiple imputation for missing data (Tables S4–S7) did not change the results for SGA or non-SGA infants.

Comment

We found that the presence of medical and obstetric risk factors for FGR was associated with significantly higher suspicion rates, but even among this higher risk group, only 40% and 60% of SGA and severely SGA infants were suspected of FGR before delivery. Moreover other well-known risk factors for FGR, including advanced maternal age, nulliparity, smoking during pregnancy and obesity were not associated with higher suspicion rates, suggesting that these factors are not used by clinicians to identify women requiring closer surveillance. Finally, fetal sex, which is a biological growth parameter and not a risk factor for poor growth, was significantly related to suspicion of FGR for both SGA and normal birthweight infants, most probably because of the use of intrauterine growth references which are not differentiated by sex.

The principal strengths of our study are that it is population-based, representative of French births, and has high-quality information on sociodemographic and clinical risk factors obtained by maternal interview and medical chart abstraction. In contrast with many studies, we were able to include false-positive infants in the analyses, and thus measured suspicion of FGR across a wide spectrum of birthweights. However, our study also has limitations. Our dependent variable, a suspicion of FGR noted in medical charts provides a synthetic measure of the antenatal assessment of fetal growth by the obstetric team and has been used in other studies.[9,11,36] We did not have information on ultrasound or fundal height measurements or on the criteria used by the team in its assessment and therefore we cannot provide further details about why FGR was not suspected (i.e. fetal weight or other biometric parameters estimated to be over the 10th percentile or measures <10th percentile, but not noted or considered important). Our findings of low suspicion are concordant with other studies using our definition of suspicion of FGR[9,11,36] as well as those using more detailed variables.[10,12,13,18,37] Finally, about 15% of data were missing in our models, but models using multiple imputation provided very similar results.

The principal factors associated with a suspicion of FGR in our study were birthweight percentile and medical/obstetric complications related to FGR.

Table 2. Medical, sociodemographic factors and health care associated with antenatal suspicion of fetal growth restriction (FGR) among small-for-gestational age (SGA) infants (<10th and <3rd percentiles)

	SGA infants <10th percentile				SGA infants <3rd percentile			
			Risks ratio (95% Cl)				Risks ratio (95% Cl)	
	N	Suspected FGR (%)	Unadjusted	Adjusted[a]	*N*	Suspected FGR (%)	Unadjusted	Adjusted[a]
Total	1219	21.7			451	33.0		
Medical/obstetric factors								
High risk of SGA	218	41.7	2.6 (2.1, 3.3)	2.1 (1.7, 2.7)	99	57.6	2.2 (1.7, 2.9)	1.9 (1.4, 2.6)
High risk (other than SGA)	98	29.6	1.7 (1.2, 2.4)	1.7 (1.2, 2.5)	35	37.1	1.4 (0.9, 2.2)	1.3 (0.8, 2.1)
Low risk	836	16.1	1.0 (Reference)	1.0 (Reference)	293	25.9	1.0 (Reference)	1.0 (Reference)
Sex								
Male	609	18.4	1.0 (Reference)	1.0 (Reference)	231	31.2	1.0 (Reference)	1.0 (Reference)
Female	610	25.1	1.4 (1.1, 1,7)	1.4 (1.1, 1.8)	220	35.0	1.1 (0.9, 1.5)	1.2 (0.9, 1.5)
Maternal age (years)								
≤19	42	28.6	1.3 (0.8, 2.1)	1.1 (0.6, 1.9)	17	35.3	1.1 (0.5, 2.1)	1.0 (0.5, 1.9)
20–34	924	22.0	1.0 (Reference)	1.0 (Reference)	331	32.6	1.0 (Reference)	1.0 (Reference)
35–39	180	20.0	0.9 (0.7, 1.2)	0.9 (0.6, 1.2)	70	32.9	1.0 (0.7, 1.4)	1.0 (0.7, 1.5)
40 +	44	20.5	0.9 (0.5, 1.7)	0.9 (0.5, 1.6)	21	33.3	1.0 (0.5, 1.9)	1.2 (0.7, 2.0)
Parity								
Nulliparous	678	20.9	1.0 (Reference)	1.0 (Reference)	236	30.1	1.0 (Reference)	1.0 (Reference)
Multiparous	531	22.4	1.1 (0.9, 1.3)	0.9 (0.7, 1.1)	210	35.7	1.2 (0.9, 1.5)	0.9 (0.7, 1.2)
Body mass index (kg/m^2)								
<18.5	151	27.2	1.3 (0.9, 1.7)	1.1 (0.8, 1.5)	57	43.9	1.4 (1.0, 2.0)	1.3 (0.9, 1.9)
18.5–24.9	742	21.3	1.0 (Reference)	1.0 (Reference)	263	30.4	1.0 (Reference)	1.0 (Reference)
25–29.9	155	16.8	0.8 (0.5, 1.1)	0.6 (0.4, 0.9)	56	32.1	1.0 (0.7, 1.6)	0.9 (0.6, 1.4)
≥30	74	27.0	1.3 (0.8, 1.9)	0.9 (0.6, 1.4)	26	46.1	1.5 (0.9, 2.4)	1.2 (0.7, 1.9)
Smoke in third trimester								
No	782	21.2	1.0 (Reference)	1.0 (Reference)	266	32.3	1.0 (Reference)	1.0 (Reference)
1–9 cigarettes/day	256	20.3	0.9 (0.7, 1.3)	0.8 (0.6, 1.1)	100	28.0	0.9 (0.6, 1.2)	0.7 (0.5, 1.0)
+10 cigarettes/day	126	25.4	1.2 (0.9, 1.7)	1.1 (0.8, 1.5)	58	39.7	1.2 (0.8, 1.8)	1.0 (0.7, 1.5)

[a]Adjusted risk ratio for all variables in the table and the birthweight ratio.

Although birthweight is not synonymous with fetal weight at ultrasound, lower weight is a major determinant of the suspicion of FGR. Medical and obstetric risk factors for FGR are well-known by clinicians who primarily use these factors to orient antenatal surveillance of FGR and to prescribe more intensive surveillance of fetal growth.[3,4,6] Pregnancies with medical and obstetric risk factors unrelated to growth restriction were also more often suspected with FGR, which may reflect the fact that these women receive more intensive surveillance, including additional visits and ultrasounds after the routine third trimester scan thereby increasing the probability of the detection of a small fetus. A recent randomized trial showed that ultrasounds later in the third trimester were more effective at detecting FGR among SGA fetuses.[18] It is also possible that in some cases, the diagnosis of the maternal condition may be a consequence of the suspicion of FGR.

Nevertheless, despite the increased rate of suspicion in the presence of medical and obstetric risk factors for FGR, more than half of women with these risk factors were not suspected of FGR when actual birthweight was below the 10th percentile, and this percentage was over 40% for infants with birthweights less than the 3rd percentile. The presence of medical and obstetric complications was also associated with a higher suspicion rate among infants born with a birthweight above the 10th percentile. Nevertheless, specificity remained high (94.7%). It is important to take specificity into consideration, as false positives may be subject to unnecessary interventions including

Table 3. Medical, sociodemographic factors and health care associated with antenatal suspicion of fetal growth restriction (FGR) among non-small-for-gestational age (SGA) infants (≥10th percentile)

	Non-SGA infants ≥10th percentile			
			Risks ratio (95% confidence interval)	
	N	Suspected FGR (%)	Unadjusted	Adjusted[a]
Total	12 881	2.1		
Medical/obstetric factors				
High risk of SGA	1 361	5.3	4.2 (3.1, 4.6)	3.7 (2.7, 5.0)
High risk (other than SGA)	1 638	4.5	3.5 (2.7, 4.7)	3.2 (2.4, 4.4)
Low risk	9 313	1.3	1.0 (Reference)	1.0 (Reference)
Sex				
Male	6 792	1.6	1.0 (Reference)	1.0 (Reference)
Female	6 089	2.6	1.6 (1.3, 2.0)	1.6 (1.3, 2.1)
Maternal age (years)				
≤19	294	4.8	2.2 (1.3, 3.7)	1.7 (0.9, 3.0)
20–34	9 957	2.2	1.0 (Reference)	1.0 (Reference)
35–39	1 981	1.3	0.6 (0.4, 0.9)	0.6 (0.4, 0.9)
40 +	435	1.1	0.5 (0.2, 1.3)	0.5 (0.2, 1.2)
Parity				
Nulliparous	5 396	2.2	1.0 (Reference)	1.0 (Reference)
Multiparous	7 390	2.0	0.9 (0.7, 1.1)	1.1 (0.8, 1.5)
Body mass index (kg/m^2)				
<18.5	950	4.0	1.9 (1.4, 2.8)	1.5 (1.1, 2.1)
18.5–24.9	7 811	2.0	1.0 (Reference)	1.0 (Reference)
25–29.9	2 133	1.5	0.7 (0.5, 1.0)	0.8 (0.6, 1.2)
≥30	1 232	1.5	0.7 (0.4, 1.1)	0.7 (0.4, 1.1)
Smoke in third trimester				
No	10 525	1.8	1.0 (Reference)	1.0 (Reference)
1–9 cigarettes/day	1 416	2.6	1.0 (0.7, 1.4)	0.9 (0.6, 1.3)
+10 cigarettes/day	525	4.4	1.6 (1.1, 2.4)	1.4 (0.9, 2.1)

[a]Adjusted risk ratio for all variables in the table and the birthweight ratio.

indicated early deliveries and cesarean delivery,[14] and this needs to be balanced against the benefits of suspicion for SGA infants.

Despite the fact that advanced maternal age, nulliparity and smoking are known to be associated with impaired fetal growth,[38] their presence did not increase suspicion of FGR. It may be that FGR was not suspected in the presence of these characteristics because providers believe that they are weak predictors in the population. However, this was true even for women smoking 10 cigarettes or more per day during their third trimester, a tobacco consumption threshold considered to have a major effect on growth.[38] It is also possible that some medical teams do not ask women about their smoking habits, or that women are reticent to admit that they smoke. In guidelines from the UK and New Zealand, additional ultrasounds are recommended for smokers.[4,6] However, in these two countries, there is no routine third trimester ultrasound. We also found that low maternal BMI was significantly related to suspicion of FGR for false positives, but not for SGA infants. Low BMI is a risk factor for FGR,[26,32] as mentioned in recent guidelines on the management of pregnancies suspected for FGR.[4–6] However, women with low BMI (<18.5 kg/m^2) may also be more likely to have constitutionally smaller babies and a higher probability of being detected for FGR.

A final factor affecting suspicion of FGR for SGA and normal birthweight infants was their sex. Females are physiologically smaller than males,[39] and birthweight curves are established separately by sex for this reason. In contrast, intrauterine growth curves, used for assessment of estimated fetal weight, are not adjusted by sex.[27] Given the fact that studies have shown that males are more vulnerable than

females to the effects of restricted growth with worse perinatal outcomes in general, this bias may aggravate the adverse outcomes of males.[40] It would be possible to integrate data on fetal sex into ultrasound curves in order to improve the accuracy of biometric and estimated fetal weight assessments and thereby ensure that males have the same chance as females of being detected for FGR. This information could be mentioned on the ultrasound report only for parents who want to know their baby's sex. Other studies have also pointed to systematic biases associated with non-sex-differentiated ultrasound references, in particular, as regards gestational age determination in Sweden where the dating ultrasound is carried out between 16 and 20 weeks.[41]

It appears that screening for FGR during pregnancy has poor performance even in a context where women receive an average of five ultrasounds during their pregnancy and that new strategies should be considered. There may be a margin for progress by increasing awareness among clinicians by education and improving surveillance protocols for women with these risk factors. One study showed that an accredited training programme in FGR and the promotion of protocols and guidelines was associated with a reduction of stillbirths in three regions in UK.[42] Paradoxically, the existence of routine ultrasound in France may lead providers to place less emphasis on risk factor assessment. This may be one of the reasons for the lack of association between smoking and the suspicion of FGR in our study. At the time of the survey, there were no guidelines about risk factor assessment and the management of pregnancies with FGR. French national guidelines on the management of pregnancies with SGA infants were published after the survey;[5] these recommendations may improve the identification of women with risk factors for FGR requiring more surveillance. The ability of ultrasounds at 32–34 weeks to detect term SGA infants has also been questioned. A recent study in Spain found that later ultrasound at 36 weeks compared with 32 weeks had better performance for the detection of FGR (38.8% vs. 22.5% of low-risk term SGA infants detected).[18] A trial is currently underway in France on this topic.[43] Another promising strategy for improving detection is longitudinal assessments of growth based on fundal height measurements, as currently recommended in the UK.[4] Finally, carrying out systematic audits of SGA infants who are not suspected during pregnancy could improve our understanding of the factors contributing to poor detection and provide guidance for improving protocols. These audits should also include non-SGA infants suspected of FGR during pregnancy in order to improve the overall effectiveness of screening.

Conclusion

Even in the presence of major clinical and obstetric risk factors for FGR, 60% and 40% of infants with birthweights less than the 10th percentile and 3rd percentile of references were not suspected of FGR. Further, well-known sociodemographic risk factors and smoking were not associated with suspicion suggesting that these factors were not taken into consideration by medical teams. Reinforcing surveillance protocols for women with known risk factors should be explored as one strategy for improving antenatal detection of FGR. Given the reduced specificity that appears to accompany better sensitivity and the possible iatrogenic consequences, evaluation should be initiated among false positives. Finally, intrauterine references should be differenced by sex in order to eliminate the systematic bias of lower suspicion for growth restricted males.

Acknowledgements

The 2010 French Perinatal Survey and this study were funded by the Ministry of Health. We thank the Maternal and Child Health Services in each district and the department heads who agreed to have the survey performed in their department. We also acknowledge the investigators who collected the data in each maternity ward. Inserm Unit 1153 has received a grant from the Bettencourt Foundation (Coups d'élan pour la Recherche française) in support of its research activities. Isabelle Monier was supported by a research grant from The Assistance publique – Hôpitaux de Paris (AP-HP).

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Classification of medical and obstetric risk factors according to the three levels of risk using French National Health Board recommendations
Table S2. Medical, sociodemographic factors and health care associated with antenatal suspicion of FGR among SGA infants (<10th and <3rd percentiles)
Table S3. Medical, sociodemographic factors and health care associated with antenatal suspicion of FGR among non-SGA infants (≥10th percentile)
Table S4. Number of missing values for each variable for our three models
Table S5. Comparison of complete case analysis vs. multiple imputation analysis for SGA infants < 10th percentile
Table S6. Comparison of complete case analysis vs. multiple imputation analysis for SGA infants < 3rd percentile
Table S7. Comparison of complete case analysis vs. multiple imputation analysis for non-SGA infants ≥10th percentile
Table S8. Medical, sociodemographic factors and health care associated with antenatal suspicion of FGR among SGA infants < 5th percentile