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Effect of regular third-trimester ultrasound examination on antenatal detection and perinatal outcomes of small for gestational age infants

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Abstract

Objective: To assess the effect of regular third-trimester ultrasound on antenatal detection and perinatal outcomes of small for gestational age (SGA) infants.

Methods: Data from SGA infants delivered at ≥28 weeks' gestation were retrospectively studied. Each pregnancy had undergone three regular third-trimester ultrasound examinations, and data were grouped according to with or without antenatal ultrasound suspicion of fetal growth restriction (FGR). Adjusted risk ratios (aRRs) of perinatal outcomes were analysed.

Results: A total of 407 infants were included, comprising 268 (65.85%) with antenatal ultrasound suspicion of FGR. Antenatal suspicion of FGR was associated with increased risk of iatrogenic delivery (aRR 2.03, 95% confidence interval [CI] 1.31, 3.14) that included risk of preterm birth (aRR 10.61, 95% CI 1.35, 83.62) and elective caesarean section (aRR 1.306, 95% CI 1.051, 1.623). Differences in fetal death, 1-min Apgar score, and admission to neonatal intensive care unit were not statistically significant. Resuscitation risk was reduced (aRR 0.22, 95% CI 0.06, 0.79).

Conclusions: Regular use of third-trimester ultrasound in one teaching hospital in China showed satisfactory antenatal detection of FGR among SGA infants. Ultrasound suspicion of FGR was associated with higher incidence of iatrogenic deliveries, but not improved neonatal outcomes, except for reduced perinatal resuscitation.

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Introduction

Fetal growth restriction (FGR) refers to the failure of a fetus to reach its inherited growth potential, and is often associated with small for gestational age (SGA) infants. The term FGR represents the fetus whose estimated fetal weight is less than the 10^{th} percentile for gestational age (GA), whereas the term SGA describes the infant whose birth weight is less than the 10^{th} percentile for GA.[1] FGR pregnancies and SGA infants are at increased risk of adverse perinatal outcomes and childhood disorders, such as stillbirth, hypoxia, neonatal death, impaired neurological development, and metabolic and cardiovascular impairment. An FGR pregnancy, when undiagnosed and therefore unmanaged, is associated with an eight-fold increase in the risk of stillbirth compared with non-FGR pregnancies.[2] Antenatal monitoring of FGR fetuses has been shown to decrease perinatal mortality by approximately 30% in high-risk pregnancies.[3] Except for trying to determine the causes of FGR, few interventions exist to treat FGR. Thus, FGR screening has become an important part of prenatal care, generally including assessment of risk factors for FGR, measurement of fundal height, and ultrasound examination, which is often preferred in the presence of FGR-related risk factors, and when the limitation of fundal height measurements is obvious, such as cases involving maternal obesity, multiple pregnancy, and polyhydramnios. Existing studies have found that only 10–36% of SGA newborns are identified during pregnancy.[4]

The present study aim was to estimate the effect of regular third-trimester ultrasound examination on antenatal detection of FGR, and the subsequent influence on obstetric and neonatal outcomes of SGA infants in a tertiary referral medical centre in China.

Patients and methods

Study population

This retrospective observational study included data from all non-anomalous, singleton births at ≥28 weeks of gestation, delivered at Peking University People's Hospital between 1 January 2014 and 31 December 2018.

The research complied with all the relevant national regulations, institutional policies and was conducted in accordance with the tenets of the Helsinki Declaration. The study protocol was approved by the Peking University People's Hospital Human Research Ethics Committee (registration number 2018PHB072-01). All of the patients provided verbal informed consent.

Study design

Data were screened for SGA infants, and data from all SGA infants (liveborn and stillborn) were divided into two groups: (1) SGA with antenatal ultrasound suspicion of FGR (SGA + FGR); and (2) SGA without antenatal ultrasound suspicion of FGR (SGA–FGR). Data from medical records regarding prenatal care, delivery and neonatal conditions were collected.

The Chinese reference of birth weight percentile for GA was used.[5] Birth weight under the 3rd percentile was defined as severe SGA.

Each pregnancy underwent three regular third-trimester ultrasound examinations (conducted by YY, ZY, or YL), at 28–30 weeks of gestation, to detect fetal anomalies that could not be diagnosed at mid-term pregnancy, and at 34–36 and 38–40 weeks of gestation, respectively, for growth monitoring, which was one part of standard care at Peking University People's Hospital. Final decisions on antenatal suspicion of FGR were made by Professor QP. Antenatal suspicion of FGR was defined as mention of suspected FGR in the late pregnancy ultrasound reports, based on estimated fetal weight under the 10th percentile for GA according to a previous Chinese publication.[5]

Obstetric outcomes were investigated by assessing iatrogenic deliveries. Iatrogenic delivery was defined as induced labour or an elective caesarean section. Preterm iatrogenic delivery was determined. Fetal indications for iatrogenic deliveries were analysed, including FGR suspicion, fetal death, amniotic liquid/umbilical/middle cerebral artery Doppler velocimetry abnormalities, and abnormal fetal heart rate.

Neonatal outcomes included fetal death, premature infant, resuscitation (defined as positive pressure ventilation in the delivery room), Apgar score at 1 min, and admission to the neonatal intensive care unit (NICU).

General characteristics of the pregnant women and newborns were also described, including maternal age, parity, body mass index (BMI), average weight gain, medical risk factors, and newborn sex, GA and birth weight. Medical risk factors were grouped into: (1) FGR-related risk factors, including a previous history of liveborn or stillborn SGA infants, any chronic vascular diseases, such as hypertension, diabetes mellitus, renal insufficiency, autoimmune disease, cyanotic cardiac disease, and antiphospholipid syndrome;[1] (2) Other risk factors, referring to those unrelated to FGR but requiring more regular doctor visits; and (3) Low risk factors, meaning without any risk factors. Birth weight was analysed as birth-weight ratio (birth weight divided by mean birth weight for GA [using reference values]).[5]

Statistical analyses

Data are presented as n (%), mean $\pm$ SD or median, and were statistically analysed using SPSS, version 22.0 (IBM, Armonk, NY, USA). Student's t-test, χ^2-test or rank sum test were used, as appropriate. The adjusted risk ratio (aRR) was calculated using polynomial regression for each obstetric and neonatal outcome, except for fetal death, due to the small number. Potential confounders included all the maternal characteristics, infant sex and birth-weight ratio. GA and birth weight were removed from the formula because GA could be influenced by the antenatal suspicion of FGR, and then had an impact on birth weight. Considering the delay between fetal death and delivery, 2 days were subtracted from the duration of pregnancy to calculate birth-weight percentiles.[6] A P value <0.05 was considered statistically significant.

Results

During the study period, 13 802 births met the data inclusion criteria. Of these, a total of 407 infants (2.95%) were SGA, and 152 (1.10%) were severe SGA. The antenatal ultrasound detection rates of SGA and severe SGA were 65.85% (268/407) and 76.97% (117/152), respectively.

Maternal and neonatal variables, used as potential confounders in risk analyses in the 407 SGA pregnancies (SGA + FGR group, $n = 268$; SGA–FGR group, $n = 139$), are presented in Table 1. Pregnant women in the SGA + FGR group were more likely to have FGR-related risk factors than those in the SGA–FGR group (38.43% versus 17.27%; $P < 0.01$). The SGA + FGR group had a lower birth-weight ratio (median 0.76 versus 0.79; $P < 0.01$) than the SGA–FGR group. Between-group differences in maternal age, parity, BMI, and average weight gain, and in neonatal sex ratios, were not statistically significant (Table 1).

Rates of each obstetric and neonatal outcome item, and aRRs between SGA + FGR versus SGA–FGR, are shown in Table 2. The SGA + FGR group had a higher rate of iatrogenic deliveries than the SGA–FGR group (61.19% versus 41.01%; $P < 0.01$), particularly regarding preterm deliveries (27.54% versus 1.75%; $P < 0.01$) and elective caesarean section (88.10% versus 67.44%; $P < 0.01$). The only preterm iatrogenic delivery in the SGA–FGR group was for fetal death. After adjustment, antenatal ultrasound suspicion of FGR was associated with a higher risk of iatrogenic delivery (aRR 2.03, 95% confidence interval [CI] 1.31, 3.14), particularly preterm birth (aRR 10.61, 95% CI 1.35, 83.62) and elective caesarean section (aRR 1.31, 95% CI 1.05, 1.62). The rate of neonatal resuscitation in the SGA + FGR group was lower than that in the SGA–FGR group (2.24% versus 5.76%), and antenatal ultrasound suspicion of FGR was associated with a lower risk (aRR 0.22, 95% CI 0.06, 0.79).

The overall rates of caesarean section were 47.01% (126/268) in the SGA + FGR group and 30.94% (43/139) in the SGA–FGR group. Fetal indications for iatrogenic deliveries were similar between the two groups: 51.22% in the SGA + FGR group (five with umbilical/middle cerebral artery Doppler velocimetry abnormalities, 10 with abnormal fetal heart rate, 12 cases of fetal death, 13 with FGR suspicion, and 44 with oligohydramnios) versus 43.86% in the SGA–FGR group (four with abnormal fetal heart rate, four cases of fetal death, and 17 with oligohydramnios). The

Table 1. Variables used as potential confounders in 407 pregnancies resulting in SGA infants.

Variable	SGA + FGR	SGA–FGR	Statistical significance
Total, *n* (%)	268 (65.85)	139 (34.15)	
Maternal			
Age, years	31.22 ± 4.50	31.39 ± 4.03	NS
Parity	1.23 ± 0.46	1.17 ± 0.40	NS
BMI, kg/m^2	21.21 ± 3.51	20.71 ± 3.19	NS
Weight gain, kg/week	0.34	0.32	NS
Medical factors[a]			
FGR-related risk factors	103 (38.43)	24 (17.27)	
Other risk factors	83 (30.97)	49 (35.25)	
Low risk factors	82 (30.60)	66 (47.48)	$P < 0.01$
Neonatal			
Sex (male/female)	121/147	75/64	NS
Birth-weight ratio	0.76	0.79	$P < 0.01$

Data presented as *n* (%) prevalence, mean ± SD or median.
SGA, small for gestational age; FGR, fetal growth restriction; BMI, body mass index.
[a]FGR-related risk factors include patients with previous history of liveborn or stillborn SGA infants, and/or any chronic vascular disease, such as hypertension, diabetes mellitus, renal insufficiency, autoimmune disease, cyanotic cardiac disease, or antiphospholipid syndrome. Other risk factors include patients with risk factors unrelated to FGR, but requiring more regular healthcare visits. Low risk factors comprise patients without any risk factors.
NS, no statistically significant between-group differences ($P > 0.05$).

Table 2. Rates and adjusted risk ratios for obstetric and neonatal outcomes in 407 pregnancies resulting in SGA infants divided into those with or without ultrasound suspicion of FGR.

Variable	SGA+FGR ($n = 268$)	SGA–FGR ($n = 139$)	aRR (95% CI)	Statistical significance
Obstetric				
Iatrogenic delivery	164/268 (61.19)	57/139 (41.01)	2.03 (1.31, 3.14)	$P < 0.01$
<37 weeks (preterm)	46/164 (27.54)	1/57 (1.75)	10.61 (1.35, 83.62)	$P < 0.01$
Elective caesarean section[a]	111/126 (88.10)	19/43 (67.44)	1.31 (1.05, 1.62)	$P < 0.01$
Iatrogenic delivery for fetal indications	84/164 (51.22)	25/57 (43.86)	1.58 (0.79, 3.14)	NS
Neonatal				
Fetal death	12/268 (4.48)	4/139 (2.88)		NS
Premature infants (<37 weeks)	51/268 (19.03)	1/139 (0.72)	4.48 (1.29, 15.60)	$P = 0.02$
Resuscitation	6/268 (2.24)	8/139 (5.76)	0.22 (0.06, 0.79)	$P = 0.02$
Apgar score <10 at 1 min	48/268 (17.91)	20/139 (14.39)	1.50 (0.78, 2.90)	NS
Admission to NICU	80/268 (29.85)	20/139 (14.39)	1.47 (0.80, 2.67)	NS

Data presented as *n* (%) prevalence.
SGA, small for gestational age; FGR, fetal growth restriction; aRR, adjusted risk ratio; CI, confidence interval; NICU, neonatal intensive care unit.
[a]As a proportion of total caesarean sections.
NS, no statistically significant risk between-group differences ($P > 0.05$).

SGA + FGR group had numerically higher rates of fetal death (4.48% versus 2.88%), admission to the NICU (29.85% versus 14.39%), and 1-min Apgar scores < 10 (17.91% versus 14.39%) than the SGA–FGR group, but the differences were not statistically significant, and the CIs for aRR included unity (Table 2).

The SGA + FGR group had a lower mean duration of gestation (37.91 ± 2.52 versus 39.09 ± 1.48 weeks, $P < 0.01$), lower absolute birth weight (2293.47 ± 492.77 g versus 2599.78 ± 264.56 g, $P < 0.01$), higher rate of preeclampsia (56/268 [20.90%] versus 16/139 [11.51%], $P = 0.02$) and higher rate of severe FGR (117/268 [43.66%] versus 35/139 [25.18%], $P < 0.01$) than the SGA–FGR group.

Discussion

Antenatal detection of SGA

Infant weights are key in diagnosing SGA, but unfortunately, birth weight can only be accurately measured after delivery. Therefore, fetal weight estimated by ultrasonography is the best choice in identifying this high-risk condition during the prenatal period. Currently, there is evidence that the preferred screening method for SGA neonates is routine third-trimester ultrasonic fetal biometry,[7] and the recommended GA is 35^{+0} to 36^{+6} weeks.[8] The regular use of ultrasound examinations three sequential times in the third trimester at the Department of Obstetrics and Gynaecology, Peking University People's Hospital exactly covered the recommended GA for screening, and could be further used to periodically monitor growth much better than a one-time only examination. FGR was mentioned prenatally in 65.85% of the current SGA cases, which represents a high detection rate, the same as 73% of respondents in a survey of the Central Association of Obstetricians Gynaecologists members,[9] but was in contrast to other studies concluding limited benefits of routine ultrasound in the third trimester.[10]

One reason for low detection rates may be errors in fetal biometry. Measurement errors for abdominal circumference, head circumference, and femur length, which can cause substantial errors in estimated fetal weight, leading to misclassification of small or appropriate for gestational age, were assumed to be 6.93, 5.15, and 1.38 mm respectively.[11] Compared with head circumference and femur length, errors from abdominal circumference would have the strongest impact on estimated fetal weight percentile, and unfortunately, abdominal circumference measurement has the largest spread. To minimize these systematic errors and achieve high reproducibility, standardized ultrasound measurement protocols and quality control are essential.[11] At Peking University People's Hospital, all fetuses undergo general ultrasound examination, including fetal biometry, by one of three investigators (YY, ZY, or YL), each with more than 10 years' experience in the field of fetal ultrasound. Once abnormal fetal growth is suspected, the patient is transferred to Professor QP, a fetal medicine specialist, for detailed examination and a decision on whether antenatal suspicion of FGR should be reported. The high-quality scan may play a key role in the high antenatal detection rate of SGA in the present study.

Obstetric and neonatal outcomes

Higher rates of iatrogenic deliveries were observed for the SGA + FGR group in the present study, which is in keeping with the view that initiation of birth may prevent the incidence of FGR-related perinatal morbidities. However, further analysis of the indications for iatrogenic deliveries showed that differences in fetal factors were not statistically significant between the two study groups, suggesting that other high-risk medical factors might play the same important role in the decision of delivery initiation as prenatal ultrasound suspicion of FGR. Additionally, 12 fetal deaths occurred in the SGA + FGR group, compared with only four in the SGA–FGR group, although this difference was not significant. Thus, both the detection of FGR and how to manage such pregnancies during subsequent prenatal care may all impact on improving perinatal outcomes.[4]

The present study also found a higher rate of preterm births in the SGA + FGR group. There is currently no consensus on the optimal timing to deliver an FGR fetus. Emerging data has shown that pregnancy management under intimate surveillance, until it was felt that delivery should be considered without delay, does not lead to worse perinatal outcomes than early delivery, but is associated with an improvement in developmental manifestation at 2 years of age.[12] A suspected FGR fetus without Doppler abnormalities can be delivered at 39 weeks of gestation.[13] In addition to GA, the potential aetiology of FGR (if known) and other antenatal clinical findings, such as abnormal Doppler velocimetry and amniotic fluid volume, and maternal risk factors, should also be considered together in any decision about whether to initiate an iatrogenic delivery.

Higher rates of preterm birth and elective caesarean section, together with no statistically significant differences in fetal death or admission to the NICU in the present study, suggest that the main benefit of antenatal ultrasound suspicion of FGR to SGA infant outcomes remains unclear. Fewer resuscitations in the SGA + FGR group with no significant differences in Apgar score at 1 minute suggest that SGA infants without ultrasound suspicion of FGR are more likely to face acute non-reassuring fetal status during labour. A higher proportion of vaginal delivery was observed in the SGA–FGR group, which may have been accompanied by high rates of fetal distress, although the difference between the two groups was not statistically significant.

Other statements

The present study reported lower proportions of SGA and severe SGA infants (2.95% and 1.10%, respectively) than other previously published studies.[14] This may be explained in part by the fact that only non-anomalous, singleton births at or after 28 weeks of gestation were included, and the use of the Chinese reference of birth-weight percentile for GA may also have played a role.

Pregnancies with antenatal ultrasound suspicion of FGR are more likely to have FGR-related risk factors, particularly preeclampsia. FGR and preeclampsia are both placenta-mediated disorders, although the accurate underlying pathophysiology is not fully understood.[15] Preeclampsia coexists in up to one-third of cases with FGR, and is thought to be a leading cause of FGR.[16] Generally, preeclampsia is classified as early-onset or late-onset, according to the GA at onset. Interestingly, there is an emerging belief that this classification should be more dependent on the presence or absence of FGR, rather than GA.[17] Once early-onset FGR is diagnosed, the presence or absence and severity of maternal hypertensive diseases affects the intervals from diagnosis to birth and severe perinatal morbidities.[18]

In the present study, SGA + FGR pregnancies had a lower birth weight, and greater proportion of severe SGA than SGA–FGR pregnancies, which may be interpreted as the higher the severity of SGA, the more easily it is detected prenatally.

Limitations and strengths

The results of the present study may be limited by several factors, including its retrospective design and single-centre setting. Suspicion of FGR was determined only from third-trimester ultrasound reports, and the study did not include appropriate for gestational age infants with suspected FGR by antenatal ultrasound examination, which will be similarly important in evaluating the worth of ultrasound screening for SGA.

Nevertheless, the study has several strengths. It adds new evidence to the existing literature, due to the specificity in China of commonly prescribing additional ultrasounds. Based on the frequent regular use of ultrasound examinations during the third trimester, the study found a high proportion of SGA infants who were suspected to have FGR prenatally. These findings support the view that use of additional ultrasounds is beneficial for detecting SGA during pregnancy.

Conclusions

Regular and sequential use of third-trimester ultrasound in one teaching hospital in China showed a satisfactory antenatal detection rate of FGR among SGA infants. The higher incidence of iatrogenic deliveries based on this detection raises questions about increased preterm birth and elective caesarean section of SGA infants, but no obvious improved neonatal outcomes, except for reduced perinatal resuscitation. Accordingly, further research is needed to illuminate thoroughly the effect of regular use of third-trimester ultrasound examination on antenatal detection and perinatal outcomes of small for gestational age infants.

Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

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