Ultrasound Obstet Gynecol 2024; **64**: 513–520
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.27661.

Association between fetal growth restriction and stillbirth in twin compared with singleton pregnancies

A. MARTÍNEZ-VAREA[1#], S. PRASAD[2#], J. DOMENECH[3], E. KALAFAT[4], J. MORALES-ROSELLÓ[1] and A. KHALIL[2,5,6,7]

[1]*Department of Obstetrics and Gynaecology, La Fe University and Polytechnic Hospital, Valencia, Spain;* [2]*Fetal Medicine Unit, St George's University Hospitals NHS Foundation Trust, University of London, London, UK;* [3]*Department of Economics and Social Sciences, Universitat Politecnica de Valencia, Valencia, Spain;* [4]*Department of Obstetrics and Gynecology, Koç University Hospital, Istanbul, Turkey;* [5]*Vascular Biology Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK;* [6]*Twin and Multiple Pregnancy Centre for Research and Clinical Excellence, St George's University Hospital, St George's University of London, London, UK;* [7]*Fetal Medicine Unit, Liverpool Women's Hospital, Liverpool, UK*

KEYWORDS: chart; fetal death; fetal growth restriction; intrauterine demise; multiple pregnancy; singleton pregnancy; small-for-gestational age; stillbirth; twin

CONTRIBUTION

What are the novel findings of this work?
Fetal growth restriction (FGR) and small-for-gestational age (SGA) are significantly associated with increased risk of stillbirth in both twin and singleton pregnancies. In singleton pregnancies, SGA and, particularly, FGR were associated with a significantly increased likelihood of stillbirth across all gestational ages at delivery. For twin pregnancies, SGA and, especially, FGR were associated with a significantly increased risk of stillbirth across all gestational ages at delivery, but only when using twin-specific birth-weight charts.

What are the clinical implications of this work?
It is essential to identify fetuses with growth restriction in both singleton and twin pregnancies, given that they are at increased risk of stillbirth. The escalating risk of stillbirth with advancing gestation in growth-restricted singleton fetuses necessitates increased monitoring and may warrant early delivery to prevent adverse outcomes. A diagnosis of SGA or FGR using twin-specific birth-weight charts was strongly associated with stillbirth in twin pregnancies; therefore, these findings encourage their use over singleton birth-weight charts.

ABSTRACT

Objectives *Twin pregnancies are at higher risk of stillbirth compared to singletons. Fetal growth restriction (FGR) is a major cause of perinatal mortality, but its impact on twins* vs *singletons remains unclear. The primary objective of this study was to investigate the association of FGR and small-for-gestational age (SGA) with stillbirth in twin compared with singleton pregnancies. A secondary objective was to assess these associations stratified by gestational age at delivery. Furthermore, we aimed to compare the associations of FGR and SGA with stillbirth in twin pregnancies using twin-specific* vs *singleton birth-weight charts, stratified by chorionicity.*

Methods *This was a retrospective cross-sectional study of pregnancies receiving obstetric care and giving birth between 1999 and 2022 at St George's Hospital, London, UK. The exclusion criteria included triplet and higher-order pregnancies, those resulting in miscarriage or live birth at* $\leq 23+6$ *weeks, termination of pregnancy and missing data regarding birth weight or gestational age at birth. Birth-weight data were collected and FGR and SGA were defined as birth weight* $<5^{th}$ *and* $<10^{th}$ *centiles, respectively. While standard logistic regression was used for singleton pregnancies, the association of FGR and SGA with stillbirth in twin pregnancies was investigated using mixed-effects logistic regression models. For twin pregnancies, intercepts were allowed to vary for twin pairs to account for intertwin dependency. Analyses were stratified by gestational age at delivery and chorionicity. Statistical significance was set at* $P \leq 0.001$.

Results *The study included 95 342 singleton and 3576 twin pregnancies. There were 494 (0.52%) stillbirths in*

Correspondence: Prof. A. Khalil, Department of Obstetrics and Gynaecology, St George's University Hospital, University of London, Blackshaw Road, Tooting, London SW17 0QT, UK (e-mail: akhalil@sgul.ac.uk)

#A.M.-V. and S.P. contributed equally to this study.

Accepted: 18 March 2024

singleton and 41 (1.15%) stillbirths in twin pregnancies (17 dichorionic and 24 monochorionic). SGA and FGR were associated significantly with stillbirth in singleton pregnancies across all gestational ages at delivery: the odds ratios (ORs) for SGA and FGR were 2.36 ((95% CI, 1.78–3.13), P < 0.001) and 2.67 ((95% CI, 2.02–3.55), P < 0.001), respectively, for delivery before 32 weeks; 2.70 ((95% CI, 1.71–4.31), P < 0.001) and 2.82 ((95% CI, 1.78–4.47), P < 0.001), respectively, for delivery between 32 and 36 weeks; and 3.85 ((95% CI, 2.83–5.21), P < 0.001) and 4.43 ((95% CI, 3.16–6.12), P < 0.001), respectively, for delivery after 36 weeks. In twin pregnancies, when stratified by gestational age at delivery, both SGA and FGR determined by twin-specific birth-weight charts were associated with increased odds of stillbirth for those delivered before 32 weeks (SGA: OR, 3.87 (95% CI, 1.56–9.50), P = 0.003 and FGR: OR, 5.26 (95% CI, 2.11–13.01), P = 0.001), those delivered between 32 and 36 weeks (SGA: OR, 6.67 (95% CI, 2.11–20.41), P = 0.001 and FGR: OR, 9.54 (95% CI, 3.01–29.40), P < 0.001) and those delivered beyond 36 weeks (SGA: OR, 12.68 (95% CI, 2.47–58.15), P = 0.001 and FGR: OR, 23.84 (95% CI, 4.62–110.25), P < 0.001). However, the association of stillbirth with SGA and FGR in twin pregnancies was non-significant when diagnosis was based on singleton charts (before 32 weeks: SGA, P = 0.014 and FGR, P = 0.005; 32–36 weeks: SGA, P = 0.036 and FGR, P = 0.008; after 36 weeks: SGA, P = 0.080 and FGR, P = 0.063).

***Conclusion** Our study demonstrates that SGA and, especially, FGR are associated significantly with an increased risk of stillbirth across all gestational ages in singleton pregnancies, and in twin pregnancies when twin-specific birth-weight charts are used. © 2024 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Prediction and prevention of stillbirth remain a challenge for both clinicians and researchers[1–4]. Despite improvements in antenatal care, stillbirth continues to represent a significant proportion of adverse pregnancy outcomes[5,6]. In 2019, 2 million fetuses were stillborn at ≥ 28 weeks' gestation worldwide, and the global stillbirth rate was 13.9 per 1000 total births[4]. Stillbirth rates in 2019 differed among regions, ranging from 22.8 per 1000 total births in West and Central Africa, to 3.0 in North America and 2.9 in Western Europe[4]. In the USA, stillbirth affects one in 160 births[5], and approximately 21 000 fetal deaths at ≥ 20 weeks' gestation were reported in 2020[6].

Stillbirth is defined as the delivery of a fetus showing no signs of life, as indicated by the absence of pulsation of the umbilical cord, heartbeat, breathing or movement of voluntary muscles[4,7,8]. There is a lack of uniformity among countries regarding the gestational age (GA) at which stillbirth is defined[4]. While fetal death at ≥ 24 weeks' gestation qualifies in the UK[9], in the USA, the definition specifies ≥ 20 weeks' gestation[6].

Twin pregnancies are at increased risk of antenatal complications and stillbirth compared with singleton pregnancies[10,11]. Previous studies have reported that fetal growth restriction (FGR) complicates 25–47% of twin and 8% of singleton pregnancies[12–16]. Noticeably, FGR is a leading cause of stillbirth worldwide[17–25]. Nonetheless, data are scarce regarding the contribution of FGR to stillbirth risk in multiple compared with singleton pregnancies. This study aimed to establish the association of FGR and small-for-gestational age (SGA) with stillbirth in twin compared with singleton pregnancies. A secondary aim was to assess the contribution of FGR and SGA to stillbirth, stratified by GA at delivery. Furthermore, we aimed to compare the association of FGR and SGA with stillbirth in twin pregnancies using twin-specific *vs* singleton birth-weight charts, stratified by chorionicity.

METHODS

Study design, participants and data sources

This was a retrospective, cross-sectional study of all pregnant women receiving obstetric care and giving birth at St George's Hospital, London, UK, between January 1999 and December 2022. January 1999 was selected as the study initiation point as ultrasound data were systematically recorded from this point onwards. Exclusion criteria included triplet and higher-order pregnancies, those resulting in miscarriage or live birth at ≤ 23 + 6 weeks' gestation, termination of pregnancy and missing data on GA at birth or birth weight. Data on maternal and pregnancy variables, as well as study outcomes, were obtained using the electronic maternity (Euroking E3 Maternity Information System, Surrey, UK) and ultrasound (ViewPoint 5.6.8.428, ViewPoint Bildverarbeitung GmbH, Wessling, Germany) databases, while neonatal outcomes were obtained from the online neonatal electronic database (Badgernet, System C, Stratford-upon-Avon, UK).

Study variables

Data on the number of fetuses in the pregnancy, chorionicity in twin pregnancies, GA at birth or at diagnosis of stillbirth, birth weight and stillbirth were collected and assessed. In twin pregnancies, chorionicity was determined by the number of placentas, the presence or absence of the lambda sign at the junction of the intertwin membrane to the placenta and the intertwin membrane thickness at the site of placental insertion in the chorion at 11–14 weeks' gestation[26]. If the first ultrasound scan was performed after 14 weeks' gestation, chorionicity was determined by the number of placentas, thickness of the intertwin membrane and discordant fetal gender[26].

GA was determined in the first trimester by assessing the crown–rump length of the larger fetus in pregnancies

conceived naturally. In pregnancies conceived by *in-vitro* fertilization (IVF), GA was calculated according to the oocyte retrieval date or the embryonic age at fertilization[27]. After 14 weeks' gestation in non-IVF pregnancies, GA was determined from the head circumference of the larger fetus[28].

Stillbirth was defined as the recorded birth of a stillborn baby of at least 24 + 0 weeks' gestation[29]. FGR and SGA were defined as birth weight below the 5th and 10th centiles, respectively, according to Fetal Medicine Foundation weight charts[30]. FGR and SGA in twin pregnancies were additionally defined as birth weight below the 5th and 10th centiles, respectively, according to twin chorionicity-specific charts[31].

The Index of Multiple Deprivation (IMD) was used as a measure of socioeconomic status[32]. IMD provides a measure of deprivation for small areas or neighborhoods in England and is derived from information regarding income, education, employment, crime and living environment. Women were categorized into five socioeconomic groups according to the level of deprivation of their neighborhood relative to that of others[32]. The first quintile contains the most deprived areas and the fifth quintile the least deprived areas. The postcode of each pregnant woman was used to ascertain their IMD.

Statistical analysis

Continuous data were described as median and interquartile range (IQR), while categorical data variables were described as *n* (%). Comparisons between the characteristics of the study groups were performed using the Mann–Whitney *U*-test for continuous variables and Fisher's exact test for categorical variables. While standard logistic regression was used for singleton pregnancies, the association of FGR and SGA with stillbirth in twin pregnancies was investigated using mixed-effects logistic regression models. For twin pregnancies, intercepts were allowed to vary for twin pairs to account for intertwin dependency. Analyses were stratified by GA at delivery and by chorionicity. Results are reported as OR with 95% CI. Statistical significance was set at $P \leq 0.001$. Statistical analysis was carried out using R software (version 4.0.3; The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Population characteristics

After applying the exclusion criteria, 95 342 singleton and 3576 twin pregnancies (2722 dichorionic and 854 monochorionic) were included in the analysis. Stillbirth was reported in 494 (0.52%) singleton and 41 (1.15%) twin pregnancies. Of stillbirths in twin pregnancies, 17 were dichorionic and 24 were monochorionic. Data on maternal demographics and pregnancy characteristics and outcomes of the study population are shown in Table 1. Compared to women with a singleton pregnancy, women with a twin pregnancy were significantly older (median (IQR), 32 (28–35) years *vs* 34 (30–37) years, $P < 0.001$), had a higher body mass index (BMI > 25 kg/m^2: 44.8% *vs* 48.7%, $P < 0.001$), were more likely to be nulliparous (50.5% *vs* 55.4%, $P < 0.001$) and less likely to smoke (6.3% *vs* 4.7%, $P < 0.001$) or consume alcohol (5.5% *vs* 1.4%, $P < 0.001$) during the pregnancy. Additionally, compared to patients with a singleton pregnancy, women with a twin pregnancy were more likely to have a white (52.6% *vs* 60.8%, $P < 0.001$) or black (12.4% *vs* 15.8%, $P < 0.001$) ethnic background, and less likely to have an Asian (19.2% *vs* 12.7%, $P < 0.001$) or mixed (15.7% *vs* 10.6%, $P < 0.001$) ethnic background. Women with a twin pregnancy were more likely to live in the least deprived quintile (18.3% *vs* 13.9%, $P < 0.001$) and less likely to have had a spontaneous conception (50.5% *vs* 93.8%, $P < 0.001$), compared to women with a singleton pregnancy. The median GA at birth was significantly lower in twin compared with singleton pregnancies (37.0 *vs* 40.0 weeks, $P < 0.001$).

Data on maternal demographics and pregnancy characteristics of singleton and twin pregnancies resulting in stillbirth are shown in Tables S1 and S2, respectively.

Association of SGA and FGR with stillbirth

Singleton pregnancy

We stratified singleton pregnancies by GA at delivery into three groups: those delivered up to 32 weeks, between 32 and 36 weeks, and beyond 36 weeks (Table 2). Among pregnancies delivered before 32 weeks, 24.1% (146/607) of SGA cases resulted in stillbirth (OR, 2.36 (95% CI, 1.78–3.13), $P < 0.001$), while 26.1% (138/528) of FGR cases resulted in stillbirth (OR, 2.67 (95% CI, 2.02–3.55), $P < 0.001$). In pregnancies delivered between 32 and 36 weeks, the proportions of SGA and FGR fetuses which resulted in stillbirth were 4.8% (43/889; OR, 2.70 (95% CI, 1.71–4.31), $P < 0.001$) and 5.3% (38/718; OR, 2.82 (95% CI, 1.78–4.47), $P < 0.001$), respectively. For those delivered beyond 36 weeks, 0.5% (67/12 599; OR, 3.85 (95% CI, 2.83–5.21), $P < 0.001$) of SGA fetuses and 0.7% (49/7344; OR, 4.43 (95% CI, 3.16–6.12), $P < 0.001$) of FGR fetuses were stillborn.

Twin pregnancy

We analyzed the association of SGA and FGR with stillbirth in twin pregnancies, stratified by GA at delivery, chorionicity and use of singleton or twin-specific birth-weight charts (Table 3).

For all twin pregnancies delivered at < 32 weeks, both SGA and FGR determined by twin-specific charts were associated with increased odds of stillbirth, with an OR of 3.87 ((95% CI, 1.56–9.50), $P = 0.003$) and OR of 5.26 ((95% CI, 2.11–13.01), $P = 0.001$), respectively. When assessed using singleton charts, the association of stillbirth with SGA and FGR was non-significant statistically, with

Table 1 Maternal demographic characteristics and pregnancy characteristics and outcomes of twin and singleton pregnancies included in study

Parameter	*Twin pregnancy* (n = *3576*)	*Singleton pregnancy* (n = *95 342*)	P
Maternal age (years)	34 (30–37)	32 (28–35)	< 0.001
> 35 years	1280/3034 (42.2)	27 902 (29.3)	< 0.001
> 40 years	296/3034 (9.8)	5342 (5.6)	< 0.001
> 45 years	36/3034 (1.2)	346 (0.4)	< 0.001
Maternal ethnicity			
White	1986/3264 (60.8)	18 044/34 274 (52.6)	< 0.001
Black	516/3264 (15.8)	4246/34 274 (12.4)	< 0.001
Asian	416/3264 (12.7)	6588/34 274 (19.2)	< 0.001
Mixed	346/3264 (10.6)	5396/34 274 (15.7)	< 0.001
Body mass index			
> 25 kg/m^2	1354/2782 (48.7)	39 036/87 122 (44.8)	< 0.001
> 30 kg/m^2	514/2782 (18.5)	14 453/87 122 (16.6)	0.009
> 35 kg/m^2	186/2782 (6.7)	4965/87 122 (5.7)	0.027
> 40 kg/m^2	56/2782 (2.0)	1618/87 122 (1.9)	0.550
IMD*			
1st quintile	120/1566 (7.7)	8017/94 455 (8.5)	0.245
2nd quintile	392/1566 (25.0)	25 747/94 455 (27.3)	0.050
3rd quintile	480/1566 (30.7)	31 246/94 455 (33.1)	0.043
4th quintile	288/1566 (18.4)	16 322/94 455 (17.3)	0.249
5th quintile	286/1566 (18.3)	13 123/94 455 (13.9)	< 0.001
Nulliparous	1980 (55.4)	48 143 (50.5)	< 0.001
Spontaneous conception	938/1857 (50.5)	19 951/21 269 (93.8)	< 0.001
Monochorionic twin pregnancy	854 (23.9)	NA	—
Smoker during pregnancy	164/3490 (4.7)	5971/94 780 (6.3)	< 0.001
Alcohol consumed during pregnancy	22/1574 (1.4)	5282 (5.5)	< 0.001
Gestational age at birth (weeks)	37.0 (35.0–37.0)	40.0 (39.0–40.9)	< 0.001
Preterm birth			
< 37 weeks	2020 (56.5)	5977 (6.3)	< 0.001
< 32 weeks	420 (11.7)	1372 (1.4)	< 0.001
< 28 weeks	164 (4.6)	615 (0.6)	< 0.001
Birth weight (g)	2380 (1980–2699)	3360 (3025–3690)	< 0.001

Data are given as median (interquartile range), *n/N* (%) or *n* (%). *Index of Multiple Deprivation (IMD) ranges from most deprived (1st quintile) to least deprived (5th quintile). NA, not applicable.

Table 2 Association of small-for-gestational age (SGA) and fetal growth restriction (FGR) with stillbirth in singleton pregnancy, stratified by gestational age (GA) at delivery

GA at delivery	n	*Live birth*	*Stillbirth*	*OR (95% CI)*	P
< 32 weeks					
SGA	607	461 (75.9)	146 (24.1)	2.36 (1.78–3.13)	< 0.001
FGR	528	390 (73.9)	138 (26.1)	2.67 (2.02–3.55)	< 0.001
32–36 weeks					
SGA	889	846 (95.2)	43 (4.8)	2.70 (1.71–4.31)	< 0.001
FGR	718	680 (94.7)	38 (5.3)	2.82 (1.78–4.47)	< 0.001
> 36 weeks					
SGA	12 599	12 532 (99.5)	67 (0.5)	3.85 (2.83–5.21)	< 0.001
FGR	7344	7295 (99.3)	49 (0.7)	4.43 (3.16–6.12)	< 0.001

Data are given as *n* (%), unless specified otherwise. OR, odds ratio.

an OR of 3.35 ((95% CI, 1.33–9.54), $P = 0.014$) and OR of 3.81 ((95% CI, 1.55–10.24), $P = 0.005$), respectively.

These associations were more pronounced in dichorionic twin pregnancies, in which the ORs for stillbirth in SGA and FGR cases using twin-specific birth-weight charts were 7.52 ((95% CI, 2.41–25.79), $P = 0.001$) and 10.72 ((95% CI, 3.40–37.16), $P < 0.001$), respectively. On the other hand, when classified using singleton charts, the ORs for stillbirth associated with SGA and FGR were 5.38 ((95% CI, 1.61–24.40), $P = 0.012$) and 8.25 ((95% CI, 2.45–37.50), $P = 0.002$), respectively, and were not statistically significant.

In contrast, monochorionic twins showed weaker, non-significant associations with stillbirth for both SGA and FGR cases using either singleton or twin-specific birth-weight charts. In monochorionic twin pregnancies, the OR for stillbirth associated with SGA using twin birth-weight charts was 1.18 ((95% CI, 0.17–5.42), $P = 0.846$), and using singleton charts it was 1.53 ((95% CI, 0.36–7.67), $P = 0.573$). Similarly, the ORs for

Table 3 Association of fetal growth restriction (FGR) and small-for-gestational age (SGA) with stillbirth in twin pregnancy, using mixed-effects logistic regression model stratified by chorionicity and gestational age (GA) at delivery and according to whether classification was based on singleton or twin-specific birth-weight charts

GA at delivery	n	*Live birth*	*Stillbirth*	*OR (95% CI)**	P
< 32 weeks					
All twins					
SGA (twin chart)	90	80 (88.9)	10 (11.1)	3.87 (1.56–9.50)	0.003
FGR (twin chart)	72	62 (86.1)	10 (13.9)	5.26 (2.11–13.01)	0.001
SGA (singleton chart)	195	180 (92.3)	15 (7.7)	3.35 (1.33–9.54)	0.014
FGR (singleton chart)	159	145 (91.2)	14 (8.8)	3.81 (1.55–10.24)	0.005
DC twins					
SGA (twin chart)	58	50 (86.2)	8 (13.8)	7.52 (2.41–25.79)	0.001
FGR (twin chart)	45	37 (82.2)	8 (17.8)	10.72 (3.40–37.16)	< 0.001
SGA (singleton chart)	119	109 (91.6)	10 (8.4)	5.38 (1.61–24.40)	0.012
FGR (singleton chart)	92	82 (89.1)	10 (10.9)	8.25 (2.45–37.50)	0.002
MC twins					
SGA (twin chart)	32	30 (93.8)	2 (6.2)	1.18 (0.17–5.42)	0.846
FGR (twin chart)	27	25 (92.6)	2 (7.4)	1.48 (0.21–6.87)	0.643
SGA (singleton chart)	76	71 (93.4)	5 (6.6)	1.53 (0.36–7.67)	0.573
FGR (singleton chart)	67	63 (94.0)	4 (6.0)	1.16 (0.26–5.08)	0.840
32–36 weeks					
All twins					
SGA (twin chart)	118	112 (94.9)	6 (5.1)	6.67 (2.11–20.41)	0.001
FGR (twin chart)	87	81 (93.1)	6 (6.9)	9.54 (3.01–29.40)	<0.001
SGA (singleton chart)	524	513 (97.9)	11 (2.1)	5.04 (1.34–32.68)	0.036
FGR (singleton chart)	419	408 (97.4)	11 (2.6)	7.75 (2.07–50.27)	0.008
DC twins					
SGA (twin chart)	90	88 (97.8)	2 (2.2)	6.70 (0.80–56.46)	0.059
FGR (twin chart)	66	64 (97.0)	2 (3.0)	9.59 (1.14–81.06)	0.025
SGA (singleton chart)	355	353 (99.4)	2 (0.6)	0.92 (0.11–7.71)	0.934
FGR (singleton chart)	284	282 (99.3)	2 (0.7)	1.40 (0.17–11.76)	0.735
MC twins					
SGA (twin chart)	28	24 (85.7)	4 (14.3)	9.37 (2.20–37.72)	0.001
FGR (twin chart)	21	17 (81.0)	4 (19.0)	13.55 (3.12–55.94)	<0.001
SGA (singleton chart)	169	160 (94.7)	9 (5.3)	NE	—
FGR (singleton chart)	135	126 (93.3)	9 (6.7)	NE	—
> 36 weeks					
All twins					
SGA (twin chart)	122	119 (97.5)	3 (2.5)	12.68 (2.47–58.15)	0.001
FGR (twin chart)	68	65 (95.6)	3 (4.4)	23.84 (4.62–110.25)	< 0.001
SGA (singleton chart)	1017	1011 (99.4)	6 (0.6)	6.65 (1.13–125.64)	0.080
FGR (singleton chart)	740	735 (99.3)	5 (0.7)	4.75 (1.02–33.21)	0.063
DC twins					
SGA (twin chart)	107	105 (98.1)	2 (1.9)	15.55 (1.85–130.67)	0.006
FGR (twin chart)	58	56 (96.6)	2 (3.4)	30.04 (3.55–254.02)	0.001
SGA (singleton chart)	817	814 (99.6)	3 (0.4)	3.41 (0.44–68.92)	0.289
FGR (singleton chart)	596	593 (99.5)	3 (0.5)	5.79 (0.74–117.24)	0.129
MC twins					
SGA (twin chart)	15	14 (93.3)	1 (6.7)	13.54 (0.61–149.72)	0.038
FGR (twin chart)	10	9 (90.0)	1 (10.0)	21.33 (0.94–243.74)	0.016
SGA (singleton chart)	200	197 (98.5)	3 (1.5)	NE	—
FGR (singleton chart)	144	142 (98.6)	2 (1.4)	3.54 (0.34–76.47)	0.304

Data are given as *n* (%), unless specified otherwise. *Multilevel logistic regression with random intercepts for twin pairs. DC, dichorionic; MC, monochorionic; NE, not estimable due to small number of events; OR, odds ratio.

stillbirth in FGR cases using twin and singleton birth-weight charts were 1.48 ((95% CI, 0.21–6.87), $P = 0.643$) and 1.16 ((95% CI, 0.26–5.08), $P = 0.840$), respectively.

For all twin pregnancies delivered between 32 and 36 weeks, both SGA and FGR determined using twin-specific charts were associated with significantly increased odds of stillbirth, with an OR of 6.67 ((95% CI, 2.11–20.41), $P = 0.001$) and OR of 9.54 ((95% CI, 3.01–29.40), $P < 0.001$), respectively. When assessed using singleton charts, the association of stillbirth with SGA or FGR was non-significant, with an OR of 5.04 ((95% CI, 1.34–32.68), $P = 0.036$) and OR of 7.75 ((95% CI, 2.07–50.27), $P = 0.008$), respectively.

In dichorionic twin pregnancies delivered between 32 and 36 weeks, the OR for stillbirth associated with SGA using twin-specific birth-weight charts was 6.70 ((95% CI, 0.80–56.46), $P = 0.059$), and that using singleton charts was 0.92 ((95% CI, 0.11–7.71),

$P = 0.934$). Similarly, the ORs for stillbirth associated with FGR using twin or singleton birth-weight charts were 9.59 ((95% CI, 1.14–81.06), $P = 0.025$) and 1.40 ((95% CI, 0.17–11.76), $P = 0.735$), respectively. In monochorionic twin pregnancies delivered between 32 and 36 weeks, the ORs for stillbirth associated with SGA and FGR using twin birth-weight charts were 9.37 ((95% CI, 2.20–37.72), $P = 0.001$) and 13.55 ((95% CI, 3.12–55.94), $P < 0.001$), respectively.

For all twin pregnancies delivered at > 36 weeks, 2.5% of SGA cases resulted in stillbirth, with an OR of 12.68 ((95% CI, 2.47–58.15), $P = 0.001$), while 4.4% of FGR cases resulted in stillbirth, with an OR of 23.84 ((95% CI, 4.62–110.25), $P < 0.001$), when using twin-specific birth-weight charts. When analyzed using singleton charts, the association of both SGA and FGR with stillbirth was non-significant statistically, with ORs of 6.65 ((95% CI, 1.13–125.64), $P = 0.080$) and 4.75 ((95% CI, 1.02–33.21), $P = 0.063$), respectively.

For dichorionic twins delivered beyond 36 weeks, 1.9% of SGA cases resulted in stillbirth with an OR of 15.55 ((95% CI, 1.85–130.67), $P = 0.006$), while 3.4% of FGR cases resulted in stillbirth with an OR of 30.04 ((95% CI, 3.55–254.02), $P = 0.001$), when using twin-specific charts. When classified by singleton charts, both SGA (OR, 3.41 (95% CI, 0.44–68.92), $P = 0.289$) and FGR (OR, 5.79 (95% CI, 0.74–117.24), $P = 0.129$), had non-significant associations with stillbirth. For monochorionic twins delivered beyond 36 weeks, when classified by twin-specific charts, 6.7% of SGA and 10.0% of FGR cases resulted in stillbirth, with ORs of 13.54 ((95% CI, 0.61–149.72), $P = 0.038$) and 21.33 ((95% CI, 0.94–243.74), $P = 0.016$), respectively. When classified using the singleton charts, 1.5% and 1.4% of SGA and FGR cases, respectively, resulted in stillbirth; however, the odds could not be calculated for SGA due to the small number of cases.

DISCUSSION

Summary of key findings

In this large retrospective study, we performed a comprehensive analysis of the association of SGA and FGR with stillbirth in both singleton and twin pregnancies, stratified by GA at delivery and chorionicity (for twin pregnancies) with the use of singleton or twin-specific charts. In singleton pregnancies, both SGA and FGR were found to have an increasingly significant association with stillbirth with advancing GA at delivery. Twin pregnancies revealed more varied results. Overall, SGA and FGR had a stronger association with stillbirth when diagnosis was based on twin-specific birth-weight charts compared to singleton charts, across all categories for GA at delivery. The association was especially pronounced in dichorionic twins delivered at < 32 weeks, in which the odds for stillbirth were notably increased compared with monochorionic twins, indicating potentially a different mechanism that influences the risk of stillbirth.

Interpretation of study findings and comparison with published literature

We report that in singleton pregnancies, SGA and, particularly, FGR were associated with an increased likelihood of stillbirth with advancing GA. This is consistent with findings from other population-based studies[33–35]. In a large USA-based population of 3 399 816 non-anomalous singleton pregnancies, Pilliod *et al.*[33] reported that the risk of stillbirth increases with GA and is inversely related to the birth-weight centile, particularly marked in the lowest centile cohort (< 3rd centile). Similar findings were reported by Hong *et al.*[34]. This is not surprising given that the mechanism of fetal demise in FGR at term is primarily an interplay of mismatched demand and supply of a fetus with poor reserves and fragile compensatory mechanisms, and placental senescence[36–38].

Our study has shown that a diagnosis of SGA or FGR using twin-specific charts is more strongly associated with stillbirth than when using singleton charts, across all GAs. Growth trajectories in singleton and twin pregnancies are different, especially in the third trimester[39–41]. Whether this is physiological or represents a pathological lag, the mechanism is not yet well defined. Furthermore, other researchers have shown that SGA twins are less likely to have an adverse perinatal outcome compared with SGA singletons[42]. Thus, a growing body of evidence supports the use of twin-specific charts over singleton charts to monitor fetal growth in twin pregnancies[22,43–45].

Lastly, this study shows that growth restriction (either SGA or FGR) is associated with an increased likelihood of stillbirth in dichorionic compared with monochorionic twins at < 32 weeks' gestation. Overall, monochorionic twins have up to a 5-fold higher risk of fetal demise compared to dichorionic twins[46], which is largely attributable to monochorionic-specific complications such as twin-to-twin transfusion syndrome (TTTS)[47,48]. In our study, among monochorionic twins who were stillborn at < 32 weeks, 69% (9/13) of cases had factors other than growth restriction as a potential etiology for stillbirth, and > 50% of cases were affected by TTTS. Growth restriction is usually a marker of placental dysfunction as GA increases[49–52]. Interestingly, the prospective risk of stillbirth in singleton and dichorionic twins increases with gestation, concurrent with placental senescence, while the prospective risk of stillbirth in monochorionic twins is highest at < 28 weeks' gestation[53]. These observed differences point toward different magnitudes or effects of SGA and FGR in the causation of stillbirth in these pregnancies. For both dichorionic and monochorionic twin pregnancies, the absolute number of stillbirth cases was small for GA > 32 weeks; therefore, although the observed odds of stillbirth were increased, statistical significance could not be achieved. Nonetheless, it is important to note that, in the overall population of twin pregnancies, severe smallness based on twin-specific charts was more likely to be associated with stillbirth than in twins classified as small using singleton charts.

Clinical and research implications

The findings demonstrate the nuanced interplay of smallness, chorionicity and GA, highlighting the importance of tailored risk assessments and consideration of specific growth charts in understanding the risk factors associated with stillbirth in both singleton and twin pregnancies. FGR is a known risk factor for stillbirth[3,17–20,22–25,33]. Rates of both FGR and perinatal demise are increased in twin compared with singleton pregnancies[54–56]. However, data are scant regarding the contribution of growth restriction to stillbirth risk in multiple compared with singleton pregnancies.

This study underscores the importance of using appropriate growth charts for twins and suggests that twin-specific charts provide a more accurate risk assessment compared with singleton charts. Management of FGR in twin pregnancies differs according to chorionicity. In monochorionic twin pregnancies complicated by selective FGR, the demise of the smaller twin is associated with an increased risk of demise or neurological impairment of the larger twin[26,57,58]. Similarly, there is limited information on the ideal GA of delivery in dichorionic twin pregnancies complicated by FGR[59]. Further research is needed to elucidate the mechanisms behind the variation in stillbirth risk in dichorionic *vs* monochorionic twins and across GA. It is crucial to develop and validate twin-specific growth charts that account for chorionicity to enhance predictive accuracy. Moreover, it is essential to evaluate interventions for preventing stillbirth in high-risk pregnancies, especially those with SGA or FGR, including delivery timing and methods, as well as antenatal surveillance.

Strengths and limitations

The main strengths of this study include the large cohort and cross-sectional design, which enabled us to investigate the occurrence of stillbirth, a clinically significant but relatively rare pregnancy outcome stratified by GA at delivery. Additionally, the effect of growth restriction on the rate of stillbirth in twin pregnancies has been addressed using singleton and twin-specific growth charts and has been stratified by chorionicity. The limitations of our study include using birth weight instead of estimated fetal weight (EFW) to identify smallness, as EFW data were not readily available for all twin and singleton pregnancies. Secondly, in the UK, obstetric care, especially for twin pregnancies, has changed and evolved since the publication of the National Institute for Health and Care Excellence guideline on antenatal care in uncomplicated twin and triplet pregnancies in 2011[60]. Implementation was concurrent with the decline in stillbirth rates in twin pregnancies, as reported by the UK MBRRACE 2016[60,61]. Thirdly, GA at delivery has been used as a surrogate for the time of stillbirth in singleton pregnancies. FGR itself can be associated with both spontaneous and iatrogenic preterm delivery, thereby affecting stratification by GA at delivery[62,63]. Another consideration is that the growth velocity of SGA or FGR fetuses may change with advancing gestation[64]. These dynamic changes in fetal growth profiles have been eloquently described by Deter *et al.*[65,66]. Lastly, a notable limitation is the small sample size in the subgroup of twins delivered at > 36 weeks' gestation. As most twin pregnancies are delivered by 36–37 weeks, the number of cases available for analysis in this late gestational period was small, potentially affecting the statistical power and the conclusiveness of the findings for this specific subgroup.

Conclusions

Our study demonstrates a significant association between SGA and, particularly, FGR fetuses and the increased risk of stillbirth in singleton pregnancies across all gestational ages. For twin pregnancies, when twin-specific birth-weight charts were used for diagnosis, SGA and, in particular, FGR were associated with a significantly higher risk of stillbirth across all GAs at delivery. When stratified by chorionicity, this association was significant in dichorionic twins delivered before 32 weeks and in monochorionic twins delivered between 32 and 36 weeks when using twin-specific charts, suggesting chorionicity-specific stillbirth risks. These findings highlight the importance of monitoring strategies tailored to gestational age and chorionicity, and support the practice of using twin-specific charts to effectively manage and mitigate stillbirth risk in twin pregnancies complicated by SGA or FGR.

REFERENCES

1. Hirst JE, Villar J, Victora CG, et al. The antepartum stillbirth syndrome: risk factors and pregnancy conditions identified from the INTERGROWTH-21st Project. *BJOG*. 2018;125(9):1145-1153.
2. Koivu A, Sairanen M. Predicting risk of stillbirth and preterm pregnancies with machine learning. *Health Inf Sci Syst*. 2020;8(1):14.
3. Ego A, Monier I, Skaare K, Zeitlin J. Antenatal detection of fetal growth restriction and risk of stillbirth: population-based case-control study. *Ultrasound Obstet Gynecol*. 2020;55(5):613-620.
4. Hug L, You D, Blencowe H, et al. Global, regional, and national estimates and trends in stillbirths from 2000 to 2019: a systematic assessment. *Lancet*. 2021;398(10302):772-785.
5. American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine in collaboration with, Metz TD, Berry RS, Fretts RC, Reddy UM, Turrentine MA. Obstetric care consensus #10: management of stillbirth: (replaces practice bulletin number 102, March 2009). *Am J Obstet Gynecol*. 2020;222(3):B2-B20.
6. Gregory EC, Valenzuela CP, Hoyert DL. Fetal mortality: United States, 2020. *Natl Vital Stat Rep*. 2022;71(4):1-20.
7. Smith GCS, Yu CKH, Papageorghiou AT, Cacho AM, Nicolaides KH, Fetal Medicine Foundation Second Trimester Screening Group. Maternal uterine artery Doppler flow velocimetry and the risk of stillbirth. *Obstet Gynecol*. 2007;109(1):144-151.
8. MacDorman MF, Gregory ECW. Fetal and perinatal mortality: United States, 2013. *Natl Vital Stat Rep*. 2015;64(8):1-24.
9. Stillbirth. nhs.uk. 2018 Accessed February 2, 2024. https://www.nhs.uk/conditions/stillbirth/
10. Mathews TJ, MacDorman MF. Infant mortality statistics from the 2008 period linked birth/infant death data set. *Natl Vital Stat Rep*. 2012;60(5):1-27.
11. Page JM, Pilliod RA, Snowden JM, Caughey AB. The risk of stillbirth and infant death by each additional week of expectant management in twin pregnancies. *Am J Obstet Gynecol*. 2015;212(5):630.e1-7.
12. Fox NS, Rebarber A, Klauser CK, Roman AS, Saltzman DH. Intrauterine growth restriction in twin pregnancies: incidence and associated risk factors. *Am J Perinatol*. 2011;28(4):267-272.
13. Reforma LG, Febres-Cordero D, Trochtenberg A, Modest AM, Collier AY, Spiel MH. Incidence of small-for-gestational-age infant birthweight following early intertwin fetal growth discordance in dichorionic and monochorionic twin pregnancies. *Am J Obstet Gynecol*. 2022;226(5):726.e1-726.e9.
14. Liu J, Wang XF, Wang Y, Wang HW, Liu Y. The incidence rate, high-risk factors, and short- and long-term adverse outcomes of fetal growth restriction: a report from Mainland China. *Medicine (Baltimore)*. 2014;93(27):e210.
15. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics and the Society forMaternal-FetalMedicin. ACOG Practice Bulletin No. 204: fetal growth restriction. *Obstet Gynecol*. 2019;133(2):e97-e109.

16. Filipecka-Tyczka D, Jakiel G, Kajdy A, Rabijewski M. Is growth restriction in twin pregnancies a double challenge? – A narrative review. *J Mother Child*. 2021;24(4):24-30.
17. Cnattingius S, Haglund B, Kramer MS. Differences in late fetal death rates in association with determinants of small for gestational age fetuses: population based cohort study. *BMJ*. 1998;316(7143):1483-1487.
18. Lindqvist PG, Molin J. Does antenatal identification of small-for-gestational age fetuses significantly improve their outcome? *Ultrasound Obstet Gynecol*. 2005;25(3):258-264.
19. Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. Maternal and fetal risk factors for stillbirth: population based study. *BMJ*. 2013;346:f108.
20. Bukowski R, Hansen NI, Willinger M, et al. Fetal growth and risk of stillbirth: a population-based case-control study. *PLoS Med*. 2014;11(4):e1001633.
21. Society for Maternal-Fetal Medicine (SMFM), Martins JG, Biggio JR, Abuhamad A. Society for Maternal-Fetal Medicine Consult Series #52: diagnosis and management of fetal growth restriction: (Replaces Clinical Guideline Number 3, April 2012). *Am J Obstet Gynecol*. 2020;223(4):B2-B17.
22. Melamed N, Baschat A, Yinon Y, et al. FIGO (international Federation of Gynecology and obstetrics) initiative on fetal growth: best practice advice for screening, diagnosis, and management of fetal growth restriction. *Int J Gynaecol Obstet*. 2021;152(Suppl 1):3-57.
23. Pacora P, Romero R, Jung E, et al. Reduced fetal growth velocity precedes antepartum fetal death. *Ultrasound Obstet Gynecol*. 2021;57(6):942-952.
24. Page JM, Blue NR, Silver RM. Fetal growth and stillbirth. *Obstet Gynecol Clin North Am*. 2021;48(2):297-310.
25. King VJ, Bennet L, Stone PR, Clark A, Gunn AJ, Dhillon SK. Fetal growth restriction and stillbirth: biomarkers for identifying at risk fetuses. *Front Physiol*. 2022;13:959750.
26. Khalil A, Rodgers M, Baschat A, et al. ISUOG Practice Guidelines: role of ultrasound in twin pregnancy. *Ultrasound Obstet Gynecol*. 2016;47(2):247-263.
27. Robinson HP, Fleming JE. A critical evaluation of sonar "crown-rump length" measurements. *Br J Obstet Gynaecol*. 1975;82(9):702-710.
28. Dias T, Ladd S, Mahsud-Dornan S, Bhide A, Papageorghiou AT, Thilaganathan B. Systematic labeling of twin pregnancies on ultrasound. *Ultrasound Obstet Gynecol*. 2011;38(2):130-133.
29. Jardine J, Walker K, Gurol-Urganci I, et al. Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study. *Lancet*. 2021;398(10314):1905-1912.
30. Nicolaides KH, Wright D, Syngelaki A, Wright A, Akolekar R. Fetal Medicine Foundation fetal and neonatal population weight charts. *Ultrasound Obstet Gynecol*. 2018;52(1):44-51.
31. Briffa C, Stirrup O, Huddy C, et al. Twin chorionicity-specific population birth-weight charts adjusted for estimated fetal weight. *Ultrasound Obstet Gynecol*. 2021;58(3):439-449.
32. English indices of deprivation 2019. GOV.UK. Accessed February 2, 2024. https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019
33. Pilliod RA, Cheng YW, Snowden JM, Doss AE, Caughey AB. The risk of intrauterine fetal death in the small-for-gestational-age fetus. *Am J Obstet Gynecol*. 2012;207(4):318.e1-6.
34. Hong J, Crawford K, Odibo AO, Kumar S. Risks of stillbirth, neonatal mortality, and severe neonatal morbidity by birthweight centiles associated with expectant management at term. *Am J Obstet Gynecol*. 2023;229(4):451.e1-451.e15.
35. Meler E, Martinez-Portilla RJ, Caradeux J, et al. Severe smallness as predictor of adverse perinatal outcome in suspected late small-for-gestational-age fetuses: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2022;60(3):328-337.
36. Heazell AEP, Crocker IP. Live and let die - regulation of villous trophoblast apoptosis in normal and abnormal pregnancies. *Placenta*. 2008;29(9):772-783.
37. Figueras F, Gratacos E. An integrated approach to fetal growth restriction. *Best Pract Res Clin Obstet Gynaecol*. 2017;38:48-58.
38. Kajdy A, Sys D, Modzelewski J, et al. Evidence of placental aging in late SGA, fetal growth restriction and stillbirth—a systematic review. *Biomedicines*. 2023;11(7):1785.
39. Stirrup OT, Khalil A, D'Antonio F, Thilaganathan B, Southwest Thames Obstetric Research Collaborative (STORK). Fetal growth reference ranges in twin pregnancy: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort. *Ultrasound Obstet Gynecol*. 2015;45(3):301-307.
40. Grantz KL, Grewal J, Albert PS, et al. Dichorionic twin trajectories: the NICHD Fetal Growth Studies. *Am J Obstet Gynecol*. 2016;215(2):221.e1-221.e16.
41. Shea SK, Likins BJ, Boan AD, Newman RB, Finneran MM. Dichorionic twin-specific vs singleton growth references for diagnosis of fetal growth restriction. *Am J Obstet Gynecol*. 2021;224(6):603.e1-603.e9.
42. Hiersch L, Barrett J, Fox NS, Rebarber A, Kingdom J, Melamed N. Should twin-specific growth charts be used to assess fetal growth in twin pregnancies? *Am J Obstet Gynecol*. 2022;227(1):10-28.
43. Mei-Dan E, Jain V, Melamed N, et al. Guideline no. 428: management of dichorionic twin pregnancies. *J Obstet Gynaecol Can*. 2022;44(7):819-834.e1.
44. Kalafat E, Sebghati M, Thilaganathan B, Khalil A, Southwest Thames Obstetric Research Collaborative (STORK). Predictive accuracy of Southwest Thames Obstetric Research Collaborative (STORK) chorionicity-specific twin growth charts for stillbirth: a validation study. *Ultrasound Obstet Gynecol*. 2019;53(2):193-199.
45. Prasad S, Khalil A. Twin charts should be the standard reference to assess growth in twin pregnancy. *Curr Opin Obstet Gynecol*. 2023;35(5):403-410.
46. Barigye O, Pasquini L, Galea P, Chambers H, Chappell L, Fisk NM. High risk of unexpected late fetal death in monochorionic twins despite intensive ultrasound surveillance: a cohort study. *PLoS Med*. 2005;2(6):e172.
47. Lee YM, Wylie BJ, Simpson LL, D'Alton ME. Twin chorionicity and the risk of stillbirth. *Obstet Gynecol*. 2008;111(2 Pt 1):301-308.
48. Russo FM, Pozzi E, Pelizzoni F, et al. Stillbirths in singletons, dichorionic and monochorionic twins: a comparison of risks and causes. *Eur J Obstet Gynecol Reprod Biol*. 2013;170(1):131-136.
49. Nardozza LMM, Caetano ACR, Zamarian ACP, et al. Fetal growth restriction: current knowledge. *Arch Gynecol Obstet*. 2017;295(5):1061-1077.
50. Burton GJ, Jauniaux E. Pathophysiology of placental-derived fetal growth restriction. *Am J Obstet Gynecol*. 2018;218(2S):S745-S761.
51. Sun C, Groom KM, Oyston C, Chamley LW, Clark AR, James JL. The placenta in fetal growth restriction: what is going wrong? *Placenta*. 2020;96:10-18.
52. Zur RL, Kingdom JC, Parks WT, Hobson SR. The placental basis of fetal growth restriction. *Obstet Gynecol Clin North Am*. 2020;47(1):81-98.
53. Glinianaia SV, Obeysekera MA, Sturgiss S, Bell R. Stillbirth and neonatal mortality in monochorionic and dichorionic twins: a population-based study. *Hum Reprod*. 2011;26(9):2549-2557.
54. Halimeh R, Melchiorre K, Thilaganathan B. Preventing term stillbirth: benefits and limitations of using fetal growth reference charts. *Curr Opin Obstet Gynecol*. 2019;31(6):365-374.
55. Khalil A, D'Antonio F, Dias T, Cooper D, Thilaganathan B, Southwest Thames Obstetric Research Collaborative (STORK). Ultrasound estimation of birth weight in twin pregnancy: comparison of biometry algorithms in the STORK multiple pregnancy cohort. *Ultrasound Obstet Gynecol*. 2014;44(2):210-220.
56. Townsend R, Khalil A. Fetal growth restriction in twins. *Best Pract Res Clin Obstet Gynaecol*. 2018;49:79-88.
57. Senat MV, Loizeau S, Couderc S, Bernard JP, Ville Y. The value of middle cerebral artery peak systolic velocity in the diagnosis of fetal anemia after intrauterine death of one monochorionic twin. *Am J Obstet Gynecol*. 2003;189(5):1320-1324.
58. Griffiths PD, Sharrack S, Chan KL, Bamfo J, Williams F, Kilby MD. Fetal brain injury in survivors of twin pregnancies complicated by demise of one twin as assessed by in utero MR imaging. *Prenat Diagn*. 2015;35(6):583-591.
59. D'antonio F, Prasad S, Masciullo L, Eltaweel N, Khalil A. Selective fetal growth restriction in dichorionic diamniotic twin pregnancy: systematic review and meta-analysis of pregnancy and perinatal outcomes. *Ultrasound Obstet Gynecol*. 2024;63(2):164-172.
60. Overview|Twin and triplet pregnancy|Guidance|NICE. NICE. 2019 Cited January 2, 2024. https://www.nice.org.uk/guidance/ng137
61. Khalil A. Unprecedented fall in stillbirth and neonatal death in twins: lessons from the UK. *Ultrasound Obstet Gynecol*. 2019;53(2):153-157.
62. Lackman F, Capewell V, Richardson B, daSilva O, Gagnon R. The risks of spontaneous preterm delivery and perinatal mortality in relation to size at birth according to fetal versus neonatal growth standards. *Am J Obstet Gynecol*. 2001;184(5):946-953.
63. Zeitlin J, Ancel PY, Saurel-Cubizolles MJ, Papiernik E. The relationship between intrauterine growth restriction and preterm delivery: an empirical approach using data from a European case-control study. *BJOG*. 2000;107(6):750-758.
64. Cody F, Unterscheider J, Daly S, et al. Dynamic growth changes in fetal growth restriction using serial ultrasonographic biometry and umbilical artery doppler: the multicenter PORTO study. *Int J Gynecol Obstet*. 2023;161(1):198-203.
65. Deter RL, Lee W, Dicker P, et al. Third-trimester growth diversity in small fetuses classified as appropriate-for-gestational age or small-for-gestational age at birth. *Ultrasound Obstet Gynecol*. 2021;58(6):882-891.
66. Deter RL, Lee W, Dicker P, et al. Growth patterns and cardiovascular abnormalities in SGA fetuses: 3. late, adaptive and recovering growth restriction. *J Matern Fetal Neonatal Med*. 2022;35(14):2808-2817.

SUPPORTING INFORMATION ON THE INTERNET

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

Table S1 Demographic characteristics and pregnancy outcomes of stillbirths and live births in singleton pregnancies

Table S2 Demographic characteristics and pregnancy outcomes of stillbirths and live births in twin pregnancies