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Letter to the Editor

Small-for-gestational age according to INTERGROWTH-21st fetal weight standard misses most pregnancies at risk of stillbirth identified by GROW

Lowering the stillbirth rate is a nationally targeted program conducted by the UK National Health Service[1], with a major focus on improving the antenatal detection of pregnancies at risk because of fetal growth restriction (FGR). Ultrasound estimation of fetal weight (EFW) is central to antenatal surveillance, yet there is no nationally agreed standard to define small-for-gestational age (SGA). The majority of hospitals in the UK use Gestation-Related Optimal Weight (GROW) charts[2] to assess fetal growth, customized to the local population and individual maternal characteristics. Most other hospitals apply INTERGROWTH-21st (IG21) charts[3], which are based on normal pregnancies averaged from eight countries.

We studied a cohort of 117 027 consecutive singleton pregnancies including 189 stillbirths (1.6 per 1000), delivered in 145 UK hospitals between January 2022 and June 2024, which had one or more third-trimester ultrasound scans with EFW performed from 28 weeks' gestation; only data from the last scan were included for cases in which more than one scan was performed. We determined the proportion of fetuses that were SGA (EFW $< 10^{th}$ centile) according to each standard (GROW and IG21), and the associated relative risk (RR) for stillbirth with 95% CI.

The median gestational age was 37 + 0 weeks at the last scan and 39 + 2 weeks at delivery. Based on EFW, the SGA rate was 7.2% according to GROW and 2.4% according to IG21 (Table 1). Most SGA cases according to IG21 ($n = 2675$) were also SGA according to GROW, and these had a RR for stillbirth of 3.8 (95% CI, 2.3–6.5). However, about twice as many additional cases ($n = 5715$) were SGA according to GROW only, and these also had an increased risk of stillbirth (RR, 1.8 (95% CI, 1.1–3.0)). These constitute 68.1% of the 8390 cases of SGA by GROW and included 50% (15/30) of the stillbirths not recognized as SGA by IG21. Cases that were SGA according to IG21 only ($n = 110$), and not by GROW, did not include any stillbirths.

Our findings indicate that the IG21 standard for SGA misses two-thirds of cases that are identified as SGA by GROW and at an increased risk of stillbirth. The reasons for this may be two-fold: first, the IG21 standard does not represent average normal fetal weight in our population; a similar conclusion was reached in a European study comparing 15 country-specific standards with the non-specific standard proposed by IG21[4]. Second, most populations are heterogeneous, with varying maternal size and ethnic group characteristics that affect fetal weight; using a fixed, one-size-fits-all standard such as IG21 that does not adjust for constitutional variation will miss fetuses that are pathologically small[5]. A coherent strategy for stillbirth prevention requires a fetal weight standard that is best able to identify the pregnancies at risk of FGR and associated stillbirth.

Table 1 Stillbirth risk associated with SGA at last scan, according to GROW *vs* IG21 standards ($n = 117\,027$; stillbirths = 189)

	SGA by GROW	*SGA by IG21*
Classified as SGA (*n* (%))	8390 (7.2)	2785 (2.4)
Stillbirths (*n* (/1000))	30 (3.6)	15 (5.4)

	SGA by GROW only	*SGA by GROW and IG21*	*SGA by IG21 only*
Classified as SGA (*n* (%))	5715 (4.9)	2675 (2.3)	110 (0.1)
Stillbirths (*n* (/1000))	15 (2.6)	15 (5.6)	0 (0)
Relative risk (95% CI)	1.8 (1.1–3.0)	3.8 (2.3–6.5)	—

GROW, Gestation-Related Optimal Weight; IG21, INTERGROWTH-21st; SGA, small-for-gestational age.

At the other end of the fetal size spectrum, IG21 was also found to be not suitable for identifying large-for-gestational age (LGA; EFW $> 90^{th}$ centile) in the same abovementioned European study[4]. While infants that were LGA by their national standard only (excluding IG21) had a significant stillbirth risk (adjusted odds ratio, 2.2 (95% CI, 1.5–3.1)), the IG21-only LGA cases had a reduced stillbirth risk (adjusted odds ratio, 0.5 (95% CI, 0.4–0.6))[4]. This confirmed findings from a geographically wider cohort of 1.25 million pregnancies from 10 countries in three continents[6], in which IG21 classified an average of 20.6% of cases as LGA - more than twice as many as GROW (9.5%); and again, such additional IG21-only cases had a reduced stillbirth risk (RR, 0.6 (95% CI, 0.5–0.7)). While IG21 misses at-risk SGA cases, a high false-positive rate of LGA is likely to lead to unnecessary investigations, interventions and parental anxiety.

In conclusion, the global one-size-fits-all hypothesis of IG21, when tested against national or individualized standards, is found wanting in its ability to identify pregnancies at risk of stillbirth.

Disclosure

All authors work for the Perinatal Institute, a not-for-profit social enterprise that developed the GROW charts used in this study.

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