

New Definition of Small for Gestational Age Based on Fetal Growth Potential

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Key Words

Birth weight · Customized assessment ·
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Small for gestational age

Abstract

Accurate definition of small for gestational age (SGA) is essential for antenatal as well as postnatal care. SGA is associated with significant antenatal and postnatal pathology. The term, however, includes constitutional smallness, and it is essential to adjust for physiological variation in order to identify those babies who are pathologically small. Maternal height, weight, parity, ethnic origin and the baby's gender have all been found to be significantly associated with normal variation in birth weight. These variables need to be adjusted for to calculate the true growth potential, which can be represented as individually customized fetal growth curves and birth weight percentiles (www.gestation.net). This method for calculating growth potential has been validated in a number of international studies. 'Customized SGA' defines neonates with intrauterine growth restriction, while 'small-normal' does not represent increased risk. Currently, coefficients are being developed for more ethnic groups, to broaden the international applicability of individualized standards. Work is also underway to incorporate the customized birth weight percentile as the starting point of infant growth curves.

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Introduction

The identification of fetuses and babies that are small for gestational age (SGA) is essential for antenatal as well as postnatal care. SGA often represents placental pathology, and may precede the clinical manifestations of pre-eclampsia, preterm labour, placental abruption, intrapartum complications or stillbirth [1, 2]. Postnatally, being SGA is significantly associated with neonatal morbidity and mortality, cerebral palsy and adverse effects in adult life [3, 4].

However, being SGA also includes constitutional smallness, and it is essential to adjust for physiological variation so as to identify those babies who are pathologically small; that is, growth restricted. Accurate assessment requires 'normal size' to be defined by the growth potential (i.e., the optimal growth of each baby). This includes the consideration of four factors.

First, accurate dating is a prerequisite for any growth standard. Ultrasound dating is much more accurate than menstrual dating. The distribution of menstrual dating error is positively skewed; many birth weight points at term therefore appear at a later gestational age than the actual gestational age, leading to an artificial flattening of the growth curve and an apparent increase in 'post-term' births [5]. In reality, growth in utero in a normal pregnancy continues without diminished velocity until birth. Dating error can also severely affect the accuracy of gestational age assessment in the preterm range.

Second, the growth standard also needs to be individually adjusted for physiological factors known to affect

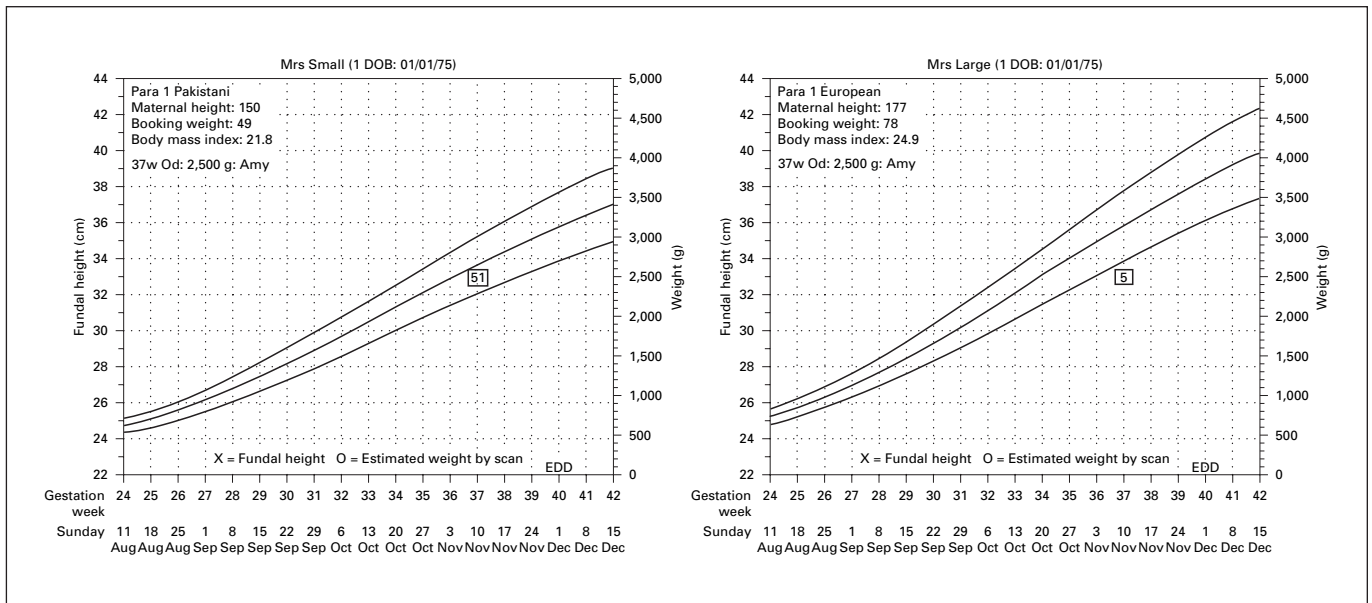


Fig. 1. Two examples of customized fetal growth curves, printed using GROW.exe version 4.6.1. The pregnancy details entered are shown on the top left, together with the (computer) calculated body mass index. The horizontal axis shows the date and month of each gestational week, calculated by the software on the basis of the expected due date entered. The charts can be used to plot previous baby weights and ultrasound-estimated fetal weight(s) in the current pregnancy. Serial fundal height measurements can also be plotted. The graphs are adjusted to predict the optimal curve for each pregnancy, based on the variables that are entered (maternal height and weight, parity, ethnic group). In the example, Mrs Small’s baby, born at 37.0 weeks and weighing 2,500 g, would be within the normal limits (51st centile), but Mrs Large’s baby, born at the same gestational age and weight, would have had intrauterine growth restriction (5th centile), as the latter’s predicted optimal growth curve is steeper.

birth weight and growth. Adjustment is required for variables including maternal height, weight in early pregnancy, parity and ethnic group, as well as the sex of the baby [6, 7]. Paternal height also plays a role, but this is relatively minor [8]. There is an infinite number of combinations of these variables, and these can be used to compute an optimal weight value at the end of a normal pregnancy (e.g., at the modal length of 280 days).

Third, the growth and birth-weight standard also needs to be free from pathology. Multivariate analysis of the constitutional variables mentioned above needs to exclude factors that are known to be associated with fetal growth abnormalities, such as smoking and diabetes.

Finally, the optimal weight at term is then combined with a ‘proportionality growth curve’, which is derived from an in-utero fetal growth formula [7]. Thus, the growth dynamics in a normal pregnancy ending with this predicted weight are outlined by a ‘gestation-related optimal weight’ curve. As a consequence of using a fetal rather than a neonatal weight-based curve, the negative skewness of birth weight curves in the preterm period are

also avoided. This skewed distribution exists because of the well-proven association between spontaneous preterm birth and fetal growth restriction [1, 9]. Because of this association, it is inappropriate to use a standard for preterm neonatal weight assessment that is derived from other preterm baby weights, as, by definition, these are abnormal.

As there is an infinite number of possible combinations to produce an optimal growth curve for an individual fetus, the calculation requires a computer. The software program (GROW – Gestation Related Optimal Weight) is available for download from www.gestation.net. Figure 1 shows two examples of individually adjusted or ‘customized’ fetal growth charts.

Evidence for Customized Assessment

An individually adjustable, customized standard for fetal growth allows better determination of whether smallness is due to a pathological condition [10]. This applies

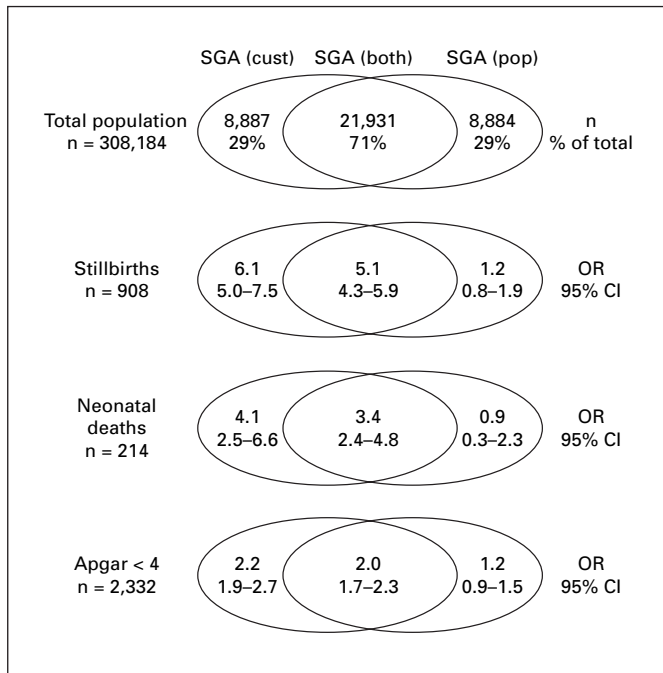


Fig. 2. Association between being small for gestational age (SGA) and adverse perinatal outcome in 308,184 Swedish births between 1992 and 1995 [19]. Outcomes are stillbirths, neonatal deaths, and low Apgar scores (<4 at 5 min). Births are grouped according to three categories: SGA births below the 10th centile by the customized standard (SGA cust) only, SGA births below the 10th centile by the population-based standard (SGA pop) only and SGA births according to both methods (SGA both). Odds ratios (ORs) compared with infants who were identified as not SGA by both standards and 95% confidence intervals are shown.

to both the antenatal assessment of estimated fetal weight and the postnatal assessment of birth weight.

Intrauterine Weight

Ultrasound-based fetal weight curves reproduce differences between physiological and constitutional characteristics, in low-risk [11] as well as high-risk [12] populations. The use of fetal weight instead of individual scan biometry parameters allows adjustment of normal intrauterine growth limits, as there are insufficient data to ‘customize’ ultrasound scan values by multivariate analysis of all the non-pathological factors that influence fetal growth. The variables can be determined from larger, population-based birth-weight databases, and then applied to intrauterine growth curves.

Customized limits reduce false-positive results for intrauterine growth restriction (IUGR) in a normal population [13]. Receiver operator curves suggest that the 10th

percentile is a suitable cut-off limit to detect those babies who will develop perinatal complications [14].

Birth Weight

When using birth weight to define SGA, it is clear that a large proportion of the population will be misclassified if an unadjusted standard is used. In a heterogeneous population, differences between ethnic groups can also be substantial [15]. Individually adjusted birth weight percentiles are better correlated with Apgar scores [6] and neonatal morphometry indices [16, 17]. They also better reflect adverse pregnancy events, even across geographical boundaries. For example, SGA defined by a customized standard derived from an English population is better correlated with operative deliveries for fetal distress and admission to neonatal intensive care in a Dutch population, than is the local Dutch population standard [18]. Also, analysis of a large Swedish dataset showed that SGA defined by a customized birth weight centile was more closely associated with stillbirths, neonatal deaths or low Apgar scores (<4) than the unadjusted population centile [19] (fig. 2). In fact, babies considered small by the general Swedish population standard but not by the customized standard did not have a larger risk of stillbirth, neonatal death or low Apgar scores than the group who had a birth weight that was appropriate for gestational age.

Further evidence has come recently from New Zealand, where investigators compared their population-based definition of SGA with an individually adjusted definition of SGA, with respect to a number of antenatal and perinatal parameters [20]. SGA by customized assessment was significantly associated with abnormal uterine and umbilical artery Doppler analysis, Caesarean section for fetal distress, a low ponderal index, hypoglycaemia, a prolonged stay in hospital, admission to the neonatal unit and overall perinatal mortality. At the same time, babies who were considered SGA by the population standard only, and not by the customized standard, did not have an increased risk of any of these outcome measures. The inference from these findings is that ‘customized’ SGA is equivalent to IUGR. Furthermore, the studies confirm that small-normal babies are not at greater risk than normal-sized babies.

Conclusion

For epidemiological analysis as well as for prospective assessment of fetal growth, individual adjustments of weight limits reduce false-positive results and help to

identify those babies who are pathologically small. This should lead to improved screening and further investigation (especially by Doppler analysis) of those babies who are at risk.

The timely detection of growth failure is important because of the ever-increasing evidence for an association between growth failure and perinatal morbidity and mortality as well as adverse effects in childhood and later life. Improvements in neonatal care and better surveillance methods for the at-risk fetus place emphasis on better screening and detection of antenatal growth problems.

Fetal biometry continues to have an important role, particularly in the third trimester when its provision of an estimated fetal weight, plotted on customized charts, will give an indication of the growth status of the fetus.

Physiological factors also need to be adjusted for when plotting the starting point of a baby's weight. Work is currently progressing to extend the same principles to charts of weight gain for neonates and children. This will allow a better distinction of whether smallness at birth and subsequent growth are normal or pathological.

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