Differentiation between normal and abnormal fetal growth

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Establishing the standard for growth

Accurate assessment of fetal growth status requires the definition of 'normal', i.e. the optimal growth of each baby. This includes the consideration of four factors which affect the standard:

1. Accurate dating is a first prerequisite for any growth standard. Ultrasound dating is much more accurate that menstrual dating. Because the distribution of menstrual dating error is positively skewed, many birth weight points at term appear at later gestations than they actually should be, leading to an artificial flattening of the growth curve and apparent increase in 'post term' births [1]. In reality, growth in utero in normal pregnancy continues without diminished velocity until birth. Dating error can also severely affect the accuracy of gestation in the preterm gestation range.

2. The growth standard also needs to be individually adjusted for physiological factors known to affect 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 [2,3]. Paternal height also plays a role but this factor is relatively minor [4]. There are an infinite number of combinations of these variables, and these can be calculated by computer to give an optimal

weight value at the end of a normal pregnancy - (e.g. at the modal length of 280 days).

3. 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 which are known to be associated with fetal growth abnormalities, such as smoking and diabetes.

4. The optimal weight at term is then combined with a 'proportionality growth curve' which is derived from an in-utero fetal growth formula [3]. Thus, the growth dynamics in a normal pregnancy ending with this predicted weight point 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. The skewed distribution exists because of the well-proven association between spontaneous preterm birth and fetal growth restriction [5]. Because of this association, it is inappropriate to use a standard for preterm neonatal weight assessment which is derived from other preterm baby weights, as by definition these are abnormal.

As there are an infinite number of possible combinations to produce an individual fetus' optimal growth curve, the method requires a computer [6]. The software program (GROW – Gestation Related Optimal Weight) is freely available for download from www.gestation.net . Figure 1 shows two examples of individually adjusted or 'customised' fetal growth charts.

Evidence for customised assessment

Application of such an individually adjustable standard for fetal growth allows better distinction between normal and abnormal smallness, and this applies both in the antenatal assessment of estimated fetal weight as well as in the postnatal assessment of birthweight.

a. Intrauterine weight

Ultrasound based fetal weight curves reproduce differences between physiological or constitutional characteristics, in low risk [7] as well as high risk [8] populations. The use of fetal weight instead of individual scan biometry parameters allows adjustment of normal intrauterine growth limits, as there is insufficient data to 'customise' ultrasound scan values by multivariate analysis of all the non-pathological factors which influence fetal growth. The variables can be determined from larger, population based birthweight databases, and then applied to intrauterine growth curves.

Customised limits reduce false positive 'IUGR' in a normal population [9]. Receiver-operator curves suggest that the 10^{th} percentile is a suitable cut-off limit to detect those babies who will develop perinatal complications [10].

b. Birth weight

When assessing small-for-gestation age (SGA) birthweight, it is clear that a large proportion of the population is misclassified if an unadjusted standard is used. In a heterogeneous population, differences between ethnic groups can also be substantial [11].

Individually adjusted birthweight percentiles are better correlated with Apgar scores [2] and neonatal morphometry indices [12,13]. They also better reflect adverse pregnancy events, even across geographical boundaries. For example, SGA defined by a customised 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 the local Dutch population standard [14]. Analysis of a large Swedish dataset showed that SGA defined by a customised birthweight centile was more closely associated with stillbirths, neonatal deaths or low Apgar scores (<4) than the unadjusted population centile [15]. In fact, babies considered small by the general Swedish population standard but not by customised standard did *not* have a larger risk of stillbirth, neonatal death or low Apgar scores than the average-for-gestational age group (Fig 2). The inference from these findings is that 'customised' SGA is equivalent to IUGR. Furthermore, this study confirms that small-normal babies are not at greater risk than normal size babies.

Conclusions

For epidemiological analysis as well as for prospective assessment of fetal growth, individual adjustments of the weight limits reduce false positives and help to identify those babies who are pathologically small. This should lead to improved screening and further investigation (especially by Doppler) of those babies who are at risk.

The timely detection of growth failure is important because of its ever-more apparent links to perinatal morbidity and mortality [16] as well as adverse effects in childhood and later life [17]. Improvements in neonatal care and better surveillance methods of the at-risk fetus place emphasis on better screening and detection of antenatal growth problems. Fetal biometry continues to have an important role, and its most effective use in the third trimester is its provision of an estimated fetal weight which, plotted on customised charts, will give an indication of the growth status of the fetus.

References

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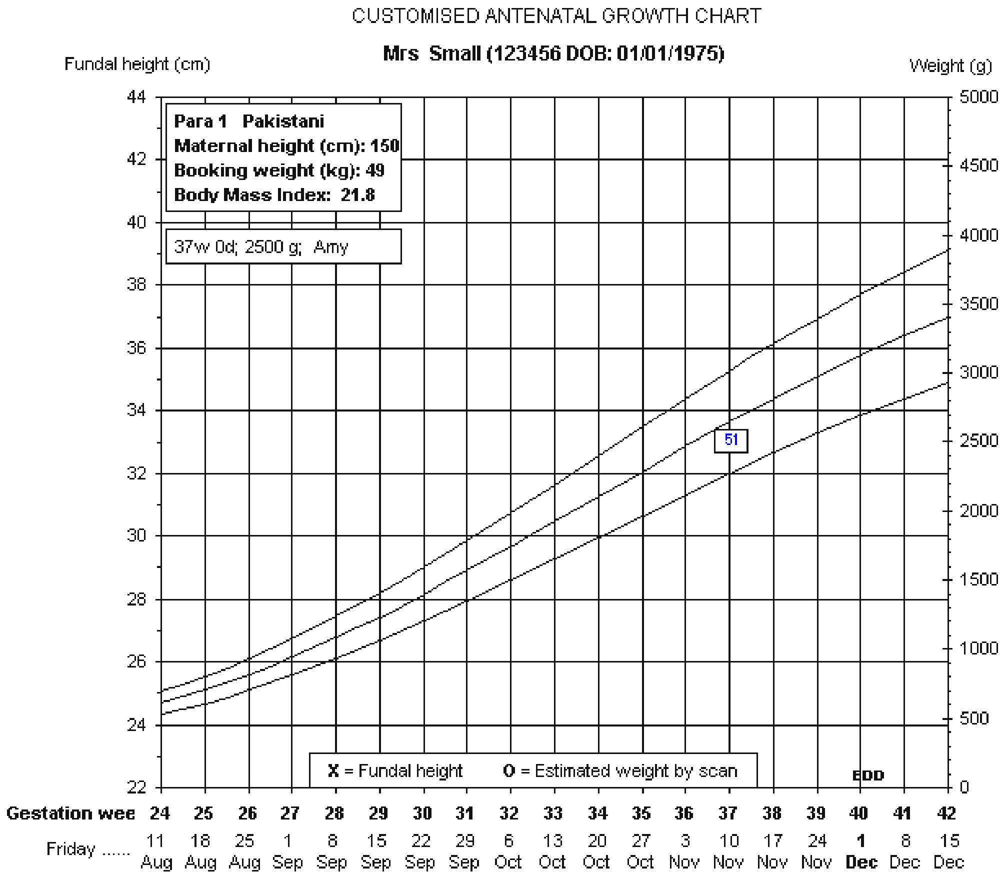
Legend to Figures 1 a & b

Two examples of customised fetal growth curves, printed out using GROW.exe version 4.6.1. 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 which are entered (maternal height and weight, parity, ethnic group).

In the example, a baby born at 37.0 weeks weighing 2500 g was within normal limits for Mrs Small (51st centile) but IUGR for Mrs Large (5th centile) as the latter's predicted optimal growth curve is steeper.

The pregnancy details entered are shown on the top left, together with the (computer-) calculated body mass index (BMI). The horizontal axis shows the day and month of each gestation week, calculated by the software on the basis of the EDD entered.


CUSTOMISED ANTENATAL GROWTH CHART
Mrs Small (123456 DOB: 01/01/1975)
Fundal height (cm)
Weight (g)
Para 1 Pakistani
Maternal height (cm): 150
Booking weight (kg): 49
Body Mass Index: 21.8
37w 0d; 2500 g; Amy
51
X = Fundal height O = Estimated weight by scan
EDD
Gestation wee
Friday ......

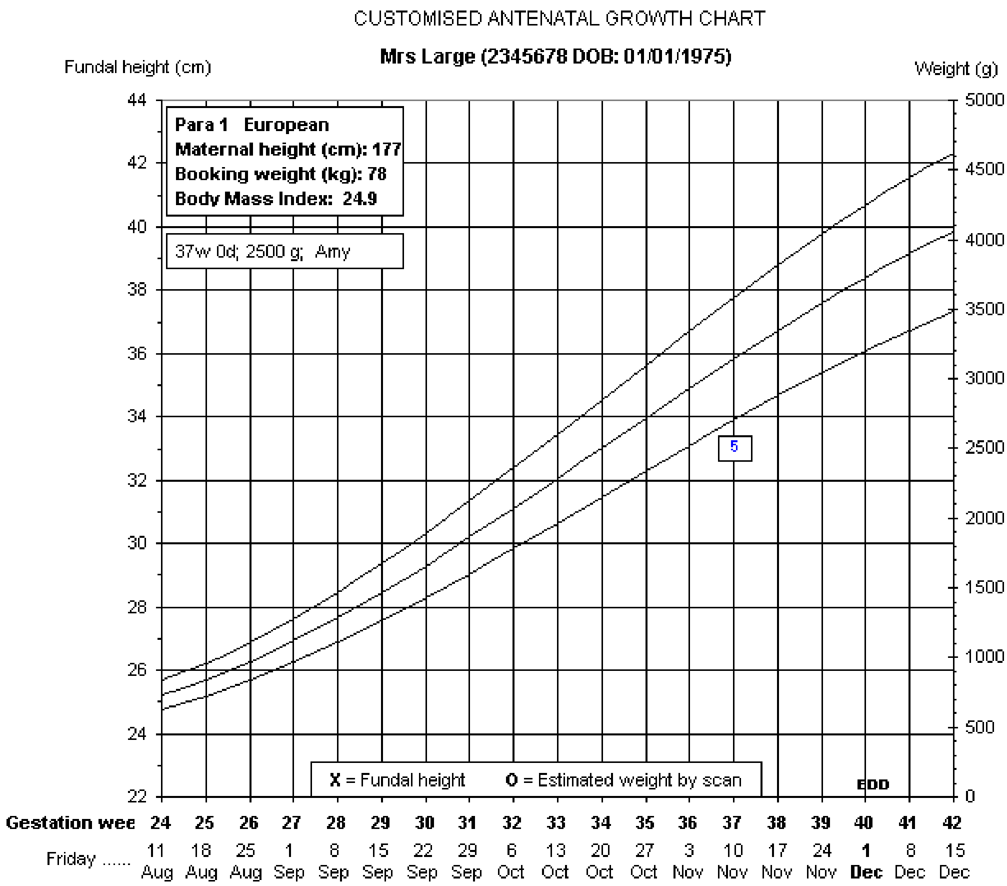

CUSTOMISED ANTENATAL GROWTH CHART
Mrs Large (2345678 DOB: 01/01/1975)
Fundal height (cm)
Weight (g)
Para 1 European
Maternal height (cm): 177
Booking weight (kg): 78
Body Mass Index: 24.9
37w 0d; 2500 g; Amy
5
X = Fundal height O = Estimated weight by scan
EDD
Gestation wee
Friday ......

Fig 2. Association between smallness-for-gestational age (SGA) and adverse perinatal outcome in 308,184 Swedish births 1992-1995 [15]. Outcomes: Stillbirths, Neonatal Deaths, and Low Apgars (< 4 at 5 minutes). Comparison between definition of SGA as lowest 10 % of births by customised percentile (SGA cust) and the lowest 10% by population based percentile (SGA pop), arranged in three categories: 1: SGA by both methods; 2: SGA by customised centile only; and 3: SGA by population percentile only. Odds ratios and 95% Confidence Intervals are shown.