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Controversy

Neonatal anthropometric charts: what they are, what they are not

E Bertino, S Milani, C Fabris, M De Curtis

Over 40 years have elapsed since Lubchenco *et al*[1] proposed an anthropometric classification of neonates based on the so-called intrauterine growth charts—that is, birth weight-for-gestational age charts.

ARE NEONATAL ANTHROPOMETRIC CHARTS INTRAUTERINE GROWTH CHARTS?

The use of charts, such as those given by Lubchenco *et al*,[1] based on the distribution of measurements taken on neonates with different gestational age, should be restricted to the auxological assessment of babies at birth. These charts, now called neonatal anthropometric charts, must not be confused with the intrauterine growth charts, which are a tool for monitoring fetal growth, based on ultrasound measurements of anthropometric traits during pregnancy: preterm births are abnormal events and preterm neonates cannot be equated to fetuses of the same gestational age who will be born at term.[2] When fetal growth studies are longitudinal, both distance and velocity intrauterine growth charts may be traced.[3 4] Strictly speaking, only charts derived from longitudinal studies should be called growth charts, growth being a process extended over time.

DOES ''SMALL-FOR-GESTATIONAL AGE'' MEAN ''INTRAUTERINE GROWTH RESTRICTED''?

The terms SGA and intrauterine growth restriction (IUGR) are often used as synonyms, although they reflect two different concepts. SGA refers to a statistical definition, based on an auxological cross-sectional evaluation (prenatal or neonatal), and denotes a fetus or a neonate whose anthropometric variables (usually weight) are lower than a given threshold value computed on a set of infants having the same gestational age. SGA includes infants who have not achieved their own growth potential, because of maternal, uterine, placental and fetal factors,[5 6] as well as small but otherwise healthy infants. IUGR refers to a clinical and functional condition and denotes fetuses unable to achieve their own growth potential: a fetus with IUGR would have been larger, without adverse environmental or genetic factors affecting growth. Such a condition can be assessed by ultrasonography during pregnancy by a longitudinal evaluation of fetal growth rate. A neonate identified as SGA by neonatal anthropometric charts is not necessarily a case of IUGR and,

conversely, a neonate identified as having IUGR during the fetal period by intrauterine growth charts may not be SGA. The current gold standard in neonatal auxological evaluation is based on information obtained from both neonatal anthropometric charts and intrauterine growth charts. Furthermore, Doppler velocimetry can detect altered flow states in the fetal–placental and uterine–placental circulation, and may contribute to the differentiation between a fetus with IUGR and a fetus who is constitutionally SGA.[7 8] When the prenatal growth pattern is unknown, SGA may be regarded as a proxy of IUGR. An alternative proxy is based on the prediction of birth weight based on early ultrasound assessments of fetal growth[9]: a negative difference between actual and predicted birth weight denotes IUGR. So far, there is insufficient evidence that this alternative method performs better than those based on fetal or neonatal charts.[10]

WHAT ABOUT RELIABILITY OF ANTHROPOMETRIC AND GESTATIONAL AGE EVALUATIONS?

Weight, length and head circumference at birth are indicators of the quality and quantity of growth: these variables must be evaluated using standardised instruments and following the techniques required for accurate measurements as described by Cameron.[11]

The validity of neonatal charts is also based on reliable estimates of gestational age, expressed as complete weeks, in accordance with international recommendations.[12] Early ultrasound assessment has improved the accuracy of estimation of gestational age,[5] and there is unanimous agreement that the best estimation is obtained by a combination of anamnestic—that is, based on reported last menstrual period—and early ultrasound assessment.[13] The a priori exclusion of neonates with unreliable gestational age seems more sensible than the a posteriori use of any statistical method for detecting biologically implausible birth weight–gestational age pairs.[12 14]

SHOULD A NEONATAL CHART BE A REFERENCE OR A STANDARD?

The target population is the population on which the chart is built and to which the chart will apply. A target population is defined by its inclusion criteria—that is, geographical area, ethnic group, sex, single birth, live birth and so on. In the absence of exclusion criteria regarding risk factors for fetal growth, a chart based on such a population is a reference, which describes ''how growth actually is'' in that population. Centers for Disease Control and Prevention growth charts for the US[15] are a reference in the sense that they are explicitly descriptive, although the authors recognise that some compromises were made on developing a true reference.[16] The two anthropometric charts elaborated by the Italian Society of Neonatology,[17 18] as well as most neonatal charts in use, are essentially descriptive references. Differences between reference charts reflect the different anthropometric characteristics of healthy neonates belonging to different populations and also the different prevalences of risk factors for prenatal growth in those populations. For this reason, by means of reference charts, the differences in the health conditions of two populations, or of one population over time, may be evaluated. On the other hand, the clinical use of a reference raises some methodological problems, as a neonate is compared with a group of peers, also including infants who may have had prenatal growth impairment; therefore, a reference might possess low sensitivity in detecting a neonate with growth anomalies. From a practical viewpoint, when the chart is based on a population with low prevalence of risk factors (such as the populations of developed countries), the clinical use of a reference can be safely accepted.

To avoid the methodological weakness of clinical use of a reference, a set of exclusion criteria can be defined, concerning mothers for example, hypertension, diabetes or renal diseases, fetuses (genetic disorders or congenital anomalies), or uterine or placental factors. Highly restrictive criteria aiming to exclude all neonates exposed to any known risk factor for intrauterine growth define the characteristics of infants who fully expressed their growth potential. Such characteristics constitute a model to which a neonate should conform, and a basis for a prescriptive standard or norm that indicates how growth should be.[16] However, there is no agreement on which diseases should be taken into consideration, and some of these may even pass unnoticed at birth. Moreover, it is rare to find neonates without IUGR with low gestational age when highly restrictive exclusion criteria are adopted, so that a norm for a severely preterm neonate may be difficult to draw. An example of neonatal standards are the Italian charts based on a multicentre survey carried out between 1973 and 1979.[19] Although these charts are the result of a noteworthy (for that time) methodological effort, they overestimate the value of anthropometric traits at low gestational age, where there is a higher probability of including infants with a true gestational age value above that assessed (at that time, ultrasound assessment of gestational age was not common obstetric practice). Even if an accurate neonatal standard were available, its clinical use could be questionable: a large proportion of severely preterm neonates have IUGR a priori,[20] and are expected to be classified as SGA on the basis of such standards. By contrast, the use of a reference, including neonates with different degrees of IUGR, enables the detection of preterm neonates having severe IUGR.

MANY LOCAL REFERENCE CHARTS OR A UNIQUE STANDARD?

A much-debated topic is whether a growth chart should be local, national or international. Strictly speaking, as a reference chart describes the anthropometry of a given population, we need as many reference charts as the number of different populations, no matter whether their anthropometric differences are ascribable to ethnic characteristics or to environmental, nutritional, socioeconomic and health conditions.

Do we really need, however, as many standards as the number of different populations? If the main reason for the differences emerging by comparison between different reference charts is the inequality in health between poor and rich populations, these differences tend to vanish when the restrictive exclusion criteria that define a standard population are adopted. In this case, only one standard could apply to all populations. The new World Health Organization child growth standards are based on such an assumption.[21] Even full-term single-born healthy infants of non-smoking mothers from a favourable socioeconomic status show a residual difference in size at birth correlated with ethnicity—for example, 1.4 cm in birth length between Norwegian and Indian neonates.[22] A unique standard is the right or the wrong choice depending on whether such differences are regarded as negligible or not. The extent to which the anthropometric differences between ethnic groups are the result of health, socioeconomic and environmental factors is still debated.[23]

As asserted by Karlberg *et al*,[24] clinicians seem to prefer local references when communicating with patients and their parents, and do not seem to take seriously any attempt to establish an international standard. Severely preterm neonates who match the requirements for a standard can hardly be found; thus, neonatal charts can be based only on a local or national reference population.

TRADITIONAL POPULATION-BASED OR CUSTOMISED CHARTS?

Establishing neonatal charts adjusted for factors permanently bound to differences in fetal growth such as sex, and single or multiple pregnancy[25 26] is indeed useful: such factors are generally taken into account to trace population-based charts. The adjustment for other covariates (the so-called customising features, such as maternal height, weight, and even maternal birth weight and birth weight of previous siblings) is gaining increasing popularity.[27–30] From a systematic review of the evidence, it seems that customised charts could be suitable to improve the detection of IUGR.[31] Nevertheless, customising features reflect constitutional factors but are also surrogates for a combination of parameters related to the mother, such as socioeconomic level and nutrition[10 30]: the available data do not permit confident inferences regarding the extent to which they induce physiological or pathological variations in fetal growth.[12]

HOW TO CHOOSE A CUT-OFF POINT TO DEFINE SGA NEONATES?

A clinically useful threshold value would discriminate neonates with IUGR, who are at high risk of short-term and long-term growth impairment, disease and death, from neonates without IUGR, who are at low risk. On inspection of neonatal morbidity and mortality ''risk maps''—that is, a kind of geographical map where prefixed levels of risk are plotted as contours as a function of gestational age (longitude) and birth weight (latitude)—it seems that neonatal risk increases with the decrease in birth weight and gestational age.[25 32] SGA neonates have long-term risk of auxological deficit,[6 33] neurocognitive impairment,[34] metabolic disorders and cardiovascular diseases.[33 35] These observations justify the use of neonatal charts, but are of no help in identifying values that best discriminate between infants at high and low risk. An alternative is to adopt statistical definitions instead of clinical ones, although the thresholds based on statistical criteria are only indirectly related to risk. In accordance with the statistical criterion, a neonate is defined to be SGA when his or her weight is below the 10th, 5th or 3rd centile of the neonatal chart or, under assumption of a gaussian distribution, 1.5 or 2 standard deviations below the average (which correspond to the centiles 6.7 and 2.3).[5] The choice of a threshold affects both sensitivity (proportion of SGA neonates among those with IUGR) and specificity (proportion of AGA neonates among those without IUGR): the use of the 3rd centile instead of the 10th centile increases specificity but decreases sensitivity. In the case of a standard based only on neonates without IUGR, setting the cut-off point at the 10th centile is the same as setting the false-positive ratio at 10%—that is, a specificity of 90%. In the case of a reference, the false-positive ratio is expected to be $<10\%$, as the reference set also includes neonates with IUGR. No univocal criterion states that one threshold is better than another, and a general agreement on the centiles to be adopted as cut-off points would be desirable.

SHOULD NEONATAL CHARTS BE UPDATED?

As regards paediatric age range, anthropometric charts should be updated every 5–10 or 15–20 years, in conformity with the intensity of the ''secular trend of growth'' in the population.[24 36] In the past 25 years, developed countries have experienced a secular trend also in birth weight.[37] Thus, more frequent updating of neonatal charts has become necessary as a result of changes not only in parity and maternal age and size but also in socioeconomic or environmental conditions, and obstetric or neonatal care.

WHAT MODELS ARE USED TO TRACE NEONATAL CHARTS?

By definition, neonatal charts are based on data from cross-sectional studies: thus, raw non-parametric centiles of the distribution of an auxometric variable conditional on gestational age show an uneven pattern when they are plotted versus age. The need to trace smooth centiles derives from the assumption that somatic growth is a continuous process, at least at a macroscopic level, and pattern irregularity is interpreted not as the expression of an underlying biological phenomenon but rather as a combined effect of measurement error and sampling variability. To trace smooth growth charts, Healy *et al*[38] introduced a class of linear models (Healy Rasbash Yang method), where the value of a given centile at a given age is expressed as polynomial function of age and z score corresponding to the centile—for example, the z score for the 3rd centile is -1.88. As an alternative, Cole[39] proposed the LMS method. This sums up the age-dependent changes in the distribution of an auxometric variable by means of three curves that represent the degree of skewness ($L(t)$), the median ($M(t)$) and the coefficient of variation ($S(t)$) at each age (t). This method permits the use of the z score even in the case of non-gaussian variables.

CONCLUSION

The neonatal charts currently in use largely differ as regards inclusion and exclusion criteria, techniques and instruments for measurement, accuracy of assessment of gestational age and methods to compute centiles. Table 1 lists several characteristics that a reliable neonatal chart should possess.

Neonatal charts traced according to the recommendations mentioned in table 1 are of both epidemiological and clinical use. From an epidemiological viewpoint, a reference neonatal chart provides a

Table 1 Characteristics that a reliable neonatal chart should possess to be of both epidemiological and clinical use

Type of survey	Pre-planned multicentre ad hoc study
Type of chart	Descriptive reference rather than an ideal prescriptive standard
Exclusion criteria	Stillbirth, major congenital anomalies
Target population	Mono-ethnic population living in a given country at a given time
Subpopulations	Females or males, single or multiple pregnancies, primiparae or multiparae
Assessment of GA	Last menstrual period confirmed by early ultrasound assessment
Range of GA	From 42 to 24 weeks or less, to cope with the increasing number of neonates with low GA
Measurements	Use of standardised instruments and measurement techniques
Technique to trace charts	HRY method[38] or LMS method[39]
Sample size	Critical sample size concerns the more external (eg, the 3rd and 97th) centiles at lower GA, therefore, attention should focus on the number of severely preterm neonates, who are more difficult to recruit. Simulation indicates that if 100 neonates are available at 24 weeks, 95% of the HRY or LMS estimates of the 3rd centile are included between centiles 1.3 and 6.3. This range narrows rapidly when GA increases (eg, at 26 weeks is between centiles 2.1 and 4.2) in the case that 100 neonates are sampled at each GA. Several neonates at term have poor effect on the precision of estimates at low GA.

HRY, Healy Rasbash Yang; GA, gestational age; LMS, lambda (skewness coefficient), mu (median), sigma (coefficient of variation).

picture of the health status of a population. The comparison of charts referring to different and clearly defined populations living in the same country or in different countries, or to the same population in different periods, is a way of measuring the extent of inequalities in health between populations or to monitor trends over time in response to public health policies.

From a clinical viewpoint, a neonatal chart is essentially a tool to detect neonates at higher risk of neonatal and postnatal morbidity and growth impairment, and to compare neonatal anthropometric conditions with those observed during postnatal growth. A comprehensive auxological evaluation of the neonate should consider not only weight, length and head circumference at birth but also fetal ultrasound biometry and Doppler velocimetry. At present, further clinical studies are needed to reach a consensus on how to combine neonatal and prenatal information to discriminate neonates with IUGR from those without IUGR.

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