

Which growth charts to use to classify neonates as small-for-gestational age at birth?

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ABSTRACT

The use of correct growth chart at birth is crucial to identify small-for-gestational age (SGA) neonates since the burden of SGA is an indicator of national health status and hence has programmatic implications. With multitude of charts available globally and in context of recent introduction of newer standard charts (Intergrowth-21st), it is important to understand the merits and demerits of different types of neonatal charts in clinical application. The current review summarizes the available growth charts and discusses the advantages and disadvantages of each of them. We conclude that most of the available growth charts either overestimate or underestimate the neonatal growth, both of which are unacceptable. Hence, it is essential to devise region specific growth charts. In case of unavailability of the regional growth charts, the global charts should be used cautiously.

Key words: Growth charts, Intrauterine growth, Neonates, Postnatal growth, Small for gestation

Small-for-gestational age (SGA) has important programmatic and research implications for newborn health and survival, particularly because 43% of under-5 deaths happen during the neonatal period. India recorded the highest number of SGA neonates, with an estimated 12.8 million neonates born SGA in our country in 2010 (95% confidence interval 11.5–14.3 million), with a prevalence of 47%. Pakistan, Nigeria, Bangladesh, China, and Indonesia had more than 1 million SGA babies [1-3].

Growth chart or centiles are the simplest tool to diagnose or define SGA neonates based on weight at birth. More than 100 growth centile charts have been published worldwide and with multitude of charts available globally, it is crucial to understand the different charts since misclassification of neonates would have huge implications on calculation of burden SGA.

A literature search on two databases (PubMed, and the Cochrane Library) using the subject headings: Neonate, (premature, very low birth weight), fetal, anthropometry, growth, birth weight, head, gestational age, newborn, growth charts, centiles, and reference values, was conducted with no defined time period, no language restrictions and foreign language articles which were translated. Articles selected included surveys of intrauterine and post-term growth. Reference lists of relevant articles were searched.

Of the 2436 citations retrieved and reviewed, 119 full-text articles were found relevant to our study and hence have been included in this review. Figure 1 provides the details of literature search.

FETAL AND NEONATAL GROWTH

Growth is defined as a net increase in size or mass of tissues as a result of either multiplication of cells or increase in intracellular substance. In context to neonatal growth, it is important to follow the growth of the neonate right from the time of conception till birth. Fetal growth, which has many determinants, both genetic and non-genetic, forms an important component of the assessment of the size of the neonate at birth. Fetal growth is assessed through anthropometric measurements by serial ultrasounds. The commonly used parameters to determine and derive fetal growth and fetal weight include the crown-rump length, head circumference (HC), femur length (FL), biparietal diameter (BPD), and abdominal circumference (AC).

The neonates' size at birth reflects the average growth rate for that neonate from conception to birth and hence may serve as a proxy measure for intrauterine growth status. Different anthropometric parameters have been used to determine the neonatal appropriateness for age, as discussed below:

Body Weight (BW)/Length/HC

Weight for gestation is used to categorize the neonates as SGA, large-for-gestational age (LGA), and appropriate-for-gestational age (AGA). Various cutoffs for size at birth are used, but the most commonly used is the 10th centile. Other criteria like Z scores (± 2 standard deviations [SD]) from the reference mean are also used.

Length provides useful additional information, as many neonates, although low weight for age, may be normal for

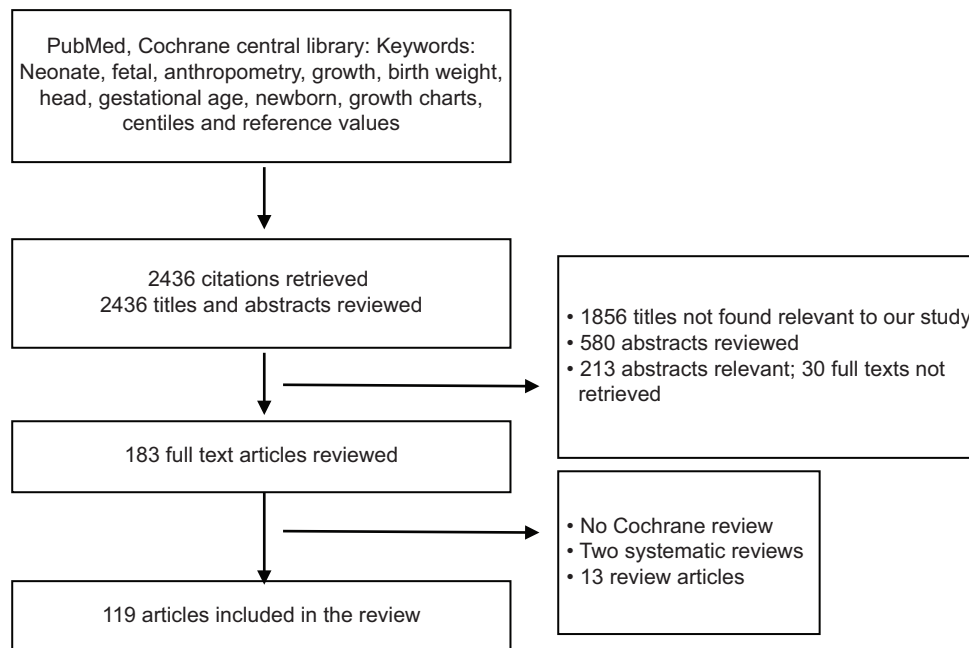


Figure 1: Flowchart depicting the literature search for the review

length, thus indicating the duration of growth restriction. However, it is measured less precisely than birth weight, and variation is more due to posture and tone of the neonate. Considerable training is also required to produce reproducible measurements.

HC can be measured more reproducibly than the birth length, although, the presence of head molding may affect its measurement. It may, however, provide important diagnostic and prognostic information beyond birth weight alone.

Proportionality Indices (Ponderal Index and Body Mass Index [BMI])

The most commonly used index is the Rohrer's ponderal index (weight in g/cube of the length). These indices may capture the timing of the growth retardation as well as nutritional status of the newborn.

Body Composition (Fat-free Mass Measurement)

Current focus for the provision of optimal nutrition is achievement of appropriate fat-free mass. Since it has been seen that providing only calories result in accumulation of fat, leading to later risk of metabolic syndrome, optimal intake of both proteins and calories is essential to build the fat-free mass. The normative values for fat-free mass are still not available for newborns.

HISTORY OF GROWTH CHARTS [4]

The idea of plotting a child's body measurements on a chart to illustrate their pattern of growth is generally attributed to Count Philibert de Montbeillard (1720–1785), who plotted his son's height every 6 months from birth to age 18 years, and George Buffon (1707–1788) then published the chart in his

Histoire Naturelle, thus producing the first height growth curve (Tanner 1962). A growth curve is a powerful graphical tool, as it displays both the size of an individual at a series of ages (gestation in case of neonate) and their growth rate or growth velocity overtime, based on the slope of the curve.

In 1929, the Fels growth study was set up in the USA, where anthropometry data were collected longitudinally overtime, and the Fels continues to this day. In 1946, the UK National Study of Health and Development was initiated, where the individuals were recruited around the time of birth and followed up through life. The 1946 Birth Cohort (Lubchenco) was followed by similar but larger cohorts in 1958, 1970, and 2000 (the Millennium Cohort) and most recently, the Intergrowth-21 Consortium charts were developed.

TYPES OF GROWTH CHARTS

A number of terminologies have been used in literature while describing the multitude of growth charts that exist currently.

Growth Reference versus Growth Standard [Table 1]

Growth reference

It is a statistical summary of anthropometry in a reference group of population and is usually presented as the frequency distribution at different ages. It is representative of a geographical region at a particular time and involves the mean and SD or alternatively the median and selected centiles, conditioned (usually) on age and sex. It describes how neonates actually grow and is used to establish whether or not their measurements are typical of the reference group. Fenton [5] charts and Lubchenco *et al.* [6] and regional charts (All India Institute of Medical Sciences [AIIMS]) [7] are examples of reference charts.

Growth standard

A growth standard is essentially the same as a growth reference except that the underlying reference sample is selected on health grounds. It represents a healthy pattern of growth. The standard shows how the neonates ought to grow rather than how they do grow. The WHO Multicenter Growth Reference Study (MGRS), 2006 [8], for term babies and the Intergrowth charts [3,9], 2014, with stringent inclusion criteria of the mothers in antenatal period are examples of the standard charts.

Regional (Local) versus Global (International) Charts

From the many charts which have been published, majority have followed the cohort from a reference population belonging to a particular region and derived the centiles, for example, Canadian standards and UK cohort study. In India, there are many different charts which have been derived from respective centers, for example, AIIMS charts, charts from Southern India. The same is true for fetal standards. Although majority of the neonatologists rely more on the regional charts, for a global comparison of the health status, it may be imperative to have a single standard curve which can be followed across all the nations. These are known as international or global charts, for example, the WHO and the Intergrowth charts.

Customized Growth Charts [10]

The customized charts, based on calculations for each individual fetus, have recently become popular on the basis of concept that each fetus has its own growth potential. Gestation-related optimal weight documentation, using the Hadlock Gardosi equation provides the term optimal weight at birth for each neonate based on the maternal height, weight, previous sibling's weight, maternal birth weight, etc. They are more suitable to detect intrauterine growth restriction (IUGR) early, but the available evidence does not give a conclusive inference about the extent to which they will influence the physiological or pathological variation in fetal growth.

In contrast to the concept of customized growth charts, all the other charts are population-based charts, with the centile representative of the reference target cohort of the neonates.

Fetal Growth Charts versus Neonatal Size at Birth/Neonatal Anthropometric versus Neonatal Postnatal Charts

In fetal curves, measurements are done during intrauterine life by ultrasounds methods. The usual fetal parameters such as the crown-rump length, BPD, FL, HC, and AC are measured during serial ultrasounds and centiles are created. The growth of the fetus is compared with the reference centile to diagnose IUGR. In neonatal anthropometric curves, measurements are done as soon as possible after birth in babies born at different gestational ages, for example, Lubchenco, Usher-McLean, and Babson curves. In the combined charts, the charts comprise the same neonates measured at birth and also during their postnatal period extended to 60 weeks post-conceptual age, for example, the Fenton meta-analysis. In the postnatal curves, growth is evaluated in a longitudinal way, i.e., by plotting consecutive increments of the different dimensions overtime, most often during the hospital stay, for example, Dancis curves and Wrights modification of Dancis and Ehrenkranz charts. Charts classified as (1), (2), and (3) are often referred to as intrauterine growth charts.

DESCRIPTION OF COMMONLY USED GROWTH CHARTS

The most commonly used charts (i) Lubchenco, (ii) WHO MGRS, and (iii) Fenton 2013 have been discussed with a brief description of the methodology used, along with the possible advantages and disadvantages of each of them.

Lubchenco (Colorado, 1967)

One of the first intrauterine charts was provided by Lubchenco, which comprised a retrospective cross-sectional multicentric study on full-term and premature infants from a period of July 1948 to January 1961, at Colorado General Hospital, USA. They all belonged to Hispanic race and the center was at high altitude. The data were collected retrospectively (from August 31, 1994, to August 9, 1995) from 26 to 42 weeks period of gestation. A total of 5635 newborns were studied, predominantly belonging to low socioeconomic status. Major congenital anomalies were

Table 1: Differences between growth reference and growth standard

S. No.	Parameter	Reference charts	Standard charts
1.	Growth pattern	They simply describe the growth of a population without taking into the consideration on health of the population	These charts provide guidance on how a neonate should grow ideally
2.	Collection of data	These charts are based on cross sectional data and hence relatively easy to acquire large sample size	These are based on prospective and longitudinal monitoring of healthy growth and hence difficult to acquire large sample size
3.	Implications on long-term outcomes, especially BMI	These charts may enable more children to be classified as normal even though overweight and obese	The standard charts have the potential to diagnose overweight and obesity early which can help in early intervention since the possible antenatal factors affecting the size at birth were excluded from the study
4.	Diagnosis of undernutrition	These charts have the potential to overdiagnose undernutrition which, in turn, can lead to overfeeding	These charts have the potential to avoid overdiagnosis of undernutrition

the exclusion criteria. Multiple pregnancies were included in the study. The gestational assessment was based on the last menstrual period. Ultrasound sonography assessment was not done. BW, length, HC, and weight length ratio (ponderal index) were measured within the first 24 h.

The percentile charts of trends and variation in length, HC, and weight length ratio with age were constructed. The 10th, 25th, 50th, 75th, and 90th centiles for each week of gestation were read from the original data, 1963, and resulting percentiles from 28 to 42 weeks of gestation were then twice smoothed by arithmetic 3-point means. The smaller number of infants at 24 and 25 weeks of gestation influenced the values below 29 weeks by the above method, and hence, the end of the curve is indicated by a broken line. The advantages were that it used ponderal index, a new parameter in charts. The disadvantages were that it was a population-based chart on one country and at high altitude; hence, centiles cannot be used globally and may not represent the global population. It was not gender based.

WHO MGRS 2006

In April 2006, the WHO released the WHO child growth standards for children aged 0 and 5 which were generated by the WHO MGRS. It was considered a milestone in the history of growth charts and has been widely used in more than 150 countries till now. MGRS is unique and unprecedented as a study in its field as the study included populations from several countries (Brazil, Ghana, India, Norway, Oman, and the USA) and it used a prescriptive approach to select the study populations, i.e., only children with minimal environmental constraints on growth were included in the study. This was achieved by recruiting children with highly educated family and good income as they have been identified as the environmental variables most likely to be associated with optimal child growth. In addition, chronic illness, failure to adhere to MGRS feeding recommendations, and maternal smoking were used as exclusion criteria. Due to these characteristics, the WHO charts provided a scientific foundation for developing standards that show how neonate should grow, as opposed to the previous studies that simply described actual patterns of growth at a particular time and place. Subsequently, these standards are now being used worldwide to judge neonatal and infant growth. The charts provide 3rd, 10th, 50th, 85th, and 97th centiles for weight, length, HC, arm circumference, and BMI from birth to 2 years.

Fenton 2013 (Meta-analysis of Six Studies and the WHO Study)

This meta-analysis was aimed to revise the 2003 Fenton Preterm Growth charts, specifically to merge the preterm growth chart with the new WHO growth standards, 2006. Six large population-based surveys of size at preterm birth representing 3968,456 (34,639 births <30 weeks) from countries Germany, the United States, Italy, Australia, Scotland, and Canada were combined in meta-analysis. Smooth growth curves were

developed, while ensuring close agreement with the data between 24 and 36 weeks and at 50 weeks.

The advantages are the centiles based on meta-analysis of seven studies, with a large number of neonates being included. Statistical methods are used to derive centiles, which overlap the WHO centiles at 50 weeks, thus can be used for postnatal monitoring also. The study provides gender-specific centiles. The disadvantages are that it is a meta-analysis of cross-sectional data, which may not reflect the true growth status, as compared to a longitudinally conducted study. Although it is widely used for postnatal monitoring also, the centiles are smoothed and derived by model-based analysis. Hence, it may not be ideal indicator of the postnatal growth pattern. Table 2 summarizes the above described international neonatal anthropometric charts.

CHARTS IN INDIAN CONTEXT [11-24]

There are several Indian studies that have generated “fetal growth” charts, based on measurements at birth at different gestational ages.

Charts by Ghosh *et al.* from Safdarjung Hospital were one of the first major charts available from India [11]. These charts were based on the length, weight, and HC from 28 to 44 weeks of gestation measured prospectively on 5000 consecutive single live born. A downward divergence was seen in the weight curves between 34 and 36 weeks as compared to the available Western growth charts (Lubchenco *et al.*, 1963), whereas a similar divergence was seen at 37–38 weeks for length and HC. This was attributed to by factors such as maternal undernutrition, anemia, and toxemia.

Similar findings were reported in a study conducted at AIIMS, New Delhi (Singh *et al.*, 1974) [25]. Another prospective study, by Mohan *et al.*, excluded babies born to diabetic or toxemic mothers [24]. Weight and length curves were noted to diverge from those of Western populations from about 35 weeks onward. Mathai *et al.* conducted a prospective study on 11,000 babies [23]. In a study by Kumar *et al.*, customization was done for maternal height as an important variable that affected birth weight, and it was observed that birth weights of Indian babies were lower than international charts across all gestational ages from 24 to 42 weeks [22]. Both 10th and 90th centiles were lower than those in Lubchenco's charts, which are commonly used for classifying neonates at birth as SGA or AGA. The authors concluded that using international rather than Indian growth charts could result in overdiagnosis of SGA and underdiagnosis of LGA babies.

LIMITATIONS OF EXISTING GROWTH CHARTS

1. Small sample sizes limited to particular regions. Only one global standard chart for preterm gestation (Intergrowth preterm charts), which has not been evaluated in our context.
2. Gestational age range different for different charts: The lower and upper limit of gestation in each chart varies with each chart. Most charts have few number of very preterm gestation neonates.

Table 2: Summary of the international neonatal anthropometric growth charts

Author	Birth years	Number	Ethnicity population	Exclusion	Estimate of GA	Interval GA (weeks)	Anthropometry
Lubchenko	1948–1961	5635	White/Denver/Colorado	Major congenital malformations	PMA	26–42	BW, length, HC, PI
Babson and Benda	1959–1963	300	White/Sea levels	Major congenital malformations	PMA	26–50	BW, length, HC
Brenner	1962–1969	30,772	White/Cleveland	None	PMA	21–44	BW
Oslen	2010	130,111	Pediatric medical group hospitals	Multiple births /congenital anomalies	Neonatologist	23	Weight, head, length
Voight	2010	2,300,000	German	None	USG	22	Weight
Kramer	2001	676,605	Canadian	-	USG	22	Weight
Roberts	1999	734,145	Australian	None	LMP/USG	20	Weight
Bonellie	2008	100,133	Scottish	None	USG/Clinician	24	Weight
Bertino	2010	45,462	Italian	None	USG	23	Weight, head, length
Zhang	1989	342,700	White/Black/USA all live births	None	PMA	22–24	BW
Thomas	1996–1998	27,229	White/Hispanic/USA	None	PMA, US, postnatal examination	22–42	BW by gender, race, altitude
Karna	1992–1997	975	White/Black/USA	Major congenital malformations	PMA, USG, postnatal measurements	23–29	BW, length, HC
Fenton (modified Babson and Benda)	2013	3986,456		None stated	USG	22–36	

GA: Gestational age, PMA: Postmenstrual age, USG: Ultrasound sonography, LMP: Last menstrual period, BW: Body weight

- Method of calculating gestational age: Non-uniform methods of gestational assessment, last menstrual period (LMP), and clinical examination, being the most commonly used methods. Intergrowth is the only chart which used strict measures of gestational assessment.
- Year of publication: Most of the regional charts being used are based on data collected more than a decade earlier and with improving newborn care and survival of low gestations getting better, it is important to review their relevance in the current scenario.
- Study design: One of the most widely used Fenton chart is based on meta-analysis and model-based derivation of the centiles. Actual prospective studies based on longitudinal follow-up are only few, Intergrowth being one of them.
- Accounting for etiological factors: Only Intergrowth took consideration of maternal characteristics and environmental factors affecting the fetal growth and ensuring their exclusion, thus accounted for possible confounders in fetal growth. All the other charts are reference charts based on cross-sectional data, without considering the etiological factors.
- Not gender specific: Most of the charts including Lubchenko and AIIMS charts being used in our context are not gender specific.
- LMP used as gestational assessment: About 40% error caused by maternal factors and error in gestation calculation as per the reported LMP.
- Preterm infants inherently different from fetus: The intrauterine growth pattern for preterm is not well defined, as preterm birth itself is pathological, as postulated, and hence, the present charts may not correctly reflect their status. A well-designed study longitudinally following the births since conception till birth may provide the closest estimate of the growth pattern. The Intergrowth study is an attempt to do the same.

Due to the limitations in the existing charts, and a dearth of growth standards which can be followed worldwide, recently, the Intergrowth-21st Consortium has provided prospective growth standards. The Intergrowth Fetal and Newborn Growth Consortium for the 21st century, in an attempt to arrive at the ideal prescriptive growth standards, provided the multicentric population-based charts [3]. The study enrolled 20,486 mothers from eligible 59,137 mothers, over a period of 5 years (April 27, 2009–March 2, 2014), from eight study sites (Brazil, Italy, Oman, the UK, the USA, China, India [Nagpur], and Kenya). These are the standard charts, with strict inclusion criteria and provide percentiles as to how the fetus should grow under ideal conditions. The mothers who were <18 years, >35 years of age, maternal height <153 cm, BMI >30 kg/m², or <18.5 kg/m² and any other illness effecting the fetal growth were excluded from the study. Indian population represented 12% of the total sample size (2493 of the 20,486 – total enrolled).

The Intergrowth-21 provides centiles in three categories:

1. Fetal Growth Longitudinal Study (FGLS) from <14+0 weeks gestational age to birth to monitor and measure fetal growth clinically (symphyseal-fundal height) and by ultrasound in a healthy population.
2. Preterm Postnatal Follow-up Study of preterm infants (>26+0 but <37+0 weeks) in the FGLS to describe their postnatal growth pattern.
3. Newborn Cross-Sectional Study of all newborns at the study centers over 12 months, obtaining anthropometric measures and neonatal morbidity and mortality rates.

Although the selection criteria and monitoring of the antenatal period were very stringent, analysis of the data raise concerns about the immediate implementation of these charts globally. There was considerable site to site variation, with the Indian fetal parameters falling below 0.5 SD across all the gestation and centile groups compared with the other seven countries. The neonatal length was the only parameter which was consistent among the eight sites, with variance <0.5 SD, but in that parameter too, Indian data (>37 weeks gestation) were at the lowest margin. Mean birth weight of the newborn (which is the most common marker taken to classify small for date) of India was 2900 g, 400 g lower compared to the total mean of 3300 g of the eight countries. The preterm delivery rate was 10% for India compared to mean of 5.5% for all the eight countries, thus indicating that perhaps Indian women do have pathologies predisposing them to preterm births, some of them having growth restriction too.

These facts indicated that population across the eight sites included in the Intergrowth centiles may not be homogenous and inter-site variations do exist due to secular trends, true ethnic differences, and different sample sizes at different gestations across all the sites.

Sri Lanka, in December 2015, became the first Southeast Asian country to implement these charts, for growth monitoring. Clinical correlates and the cutoff of the 3rd centile on Intergrowth charts to classify neonates as SGA needs to be evaluated before arriving at a consensus of implementing them in the country. More careful debate and discussion on the published and unpublished data of the Intergrowth-21st study are required before thinking of considering these as universal standards.

CLASSIFYING THE FETUS AND NEONATE ON THE BASIS OF GROWTH CHARTS

The Centiles and Z Scores for Classification of SGA [26]

Smoothed percentile curves and Z-scores are used to evaluate the growth of children. Percentiles rank the position of an individual by indicating what percentage of the reference population the individual would equal or exceed. The centile indicates the distance that they have traveled along the growth road up to that age. The growth chart quantifies size/distance in terms of the centile. A Z-score is the deviation of the value for an individual

from the mean value of the reference population divided by the SD for the reference population. Because Z-scores have a direct relationship with percentiles, a conversion can occur in either direction using a standard normal distribution table. Therefore, Z-scores and percentiles are interchangeable.

The choice to use Z-score or percentile is based primarily on convention or preference. In certain population-based applications, such as research settings and surveillance systems, the mean and SD are often calculated for a group of Z-scores. In selected clinical situations, where growth monitoring is an important evaluation tool and greater measurement precision is necessary, Z-scores or exact percentiles may be preferred by clinicians.

To track growth below the 5th percentile, Z-scores achieved widespread use. A Z-score of -2 SD is accepted as a standard statistical cutoff point to determine the need for nutritional intervention and corresponds approximately to the 3rd percentile (Z-score at 3rd percentile = 1.88) (77). Z-score (or SD score) = (Observed value - median value of reference population/SD value of reference population).

Interpreting the results in terms of Z scores has several advantages. There is same statistical relation to the distribution of the reference around the mean at all ages, which makes results comparable across age groups and indicators. Z-scores are also sex independent, thus permitting the evaluation of children growth status by combining sex and age groups. These characteristics of Z-scores allow further computation of summary statistics such as means, SDs, and standard error to classify a population's growth status. For population-based assessment, including surveys and nutritional surveillance, the Z-score is widely recognized as the best system for analysis and presentation of anthropometric data.

CONCLUSION

Both over- and underestimation of SGA is inappropriate, as the national prevalence of SGA not only is an indicator of quality of health care but also determines the interventions to be taken to improve the health care of the nation. Hence, it is important to determine the appropriate growth chart which most correctly estimates the proportion of SGA.

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