Current use and performance of the different fetal growth charts in the Italian population

Tamara Stampalija[a,b,*], Tullio Ghi[c], Valentina Rosolen[d], Giuseppe Rizzo[e,f], Enrico Maria Ferrazzi[g], Federico Prefumo[h,i], Andrea Dall'Asta[c], Mariachiara Quadrifoglio[a], Tullia Todros[j], Tiziana Frusca[c], On behalf of SIEOG working group on fetal biometric charts[1]

[a] *Unit of Fetal Medicine and Prenatal Diagnosis, Institute for Maternal and Child Health IRCCS Burlo Garofolo, Via dell'Istria 65, 34100 Trieste, Italy*
[b] *Department of Medicine, Surgery and Health Sciences, University of Trieste, Strada di Fiume 447, 34149 Trieste, Italy*
[c] *Department of Medicine and Surgery, Obstetrics and Gynecology Unit, University of Parma, Via Gramsci 14, 43125 Parma, Italy*
[d] *Clinical Epidemiology and Public Health Research Unit, Institute for Maternal and Child Health IRCCS Burlo Garofolo, Via dell'Istria 65, 34100 Trieste, Italy*
[e] *Division of Maternal Fetal Medicine, Ospedale Cristo Re, University of Rome Tor Vergata, Viale Montpelier 1, 00133 Rome, Italy*
[f] *Department of Obstetrics and Gynecology, The First I.M. Sechenov Moscow State Medical University, Moscow, Russia*
[g] *IRCCS Fondazione Ca' Granda, Policlinico di Milano, Via Francesco Sforza 28, 20122 Milano, Italy*
[h] *Division of Obstetrics and Gynecology, Department of Clinical and Experimental Sciences, University of Brescia, Piazza del Mercato 15, 25121 Brescia, Italy*
[i] *Division of Obstetrics and Gynecology, ASST Spedali Civili, P.le Spedali Civili 1, 25123 Brescia, Italy*
[j] *Department of Obstetrics and Gynaecology, Ultrasound Centre, University of Turin, Sant'Anna Hospital, Corso Spexzia 60, 10126 Turin, Italy*

A R T I C L E I N F O

Accepted 26 June 2020

Keywords:
Growth charts
Small for gestational age
Large for gestational age
Intergrowth-21
World health organization

A B S T R A C T

Objectives: The choice of growth charts impacts on screening, diagnosis and clinical management of fetal growth abnormalities. The objectives of the study were to evaluate: 1) the clinical practice at a national level among tertiary referral centers in the use of fetal biometric growth charts; and 2) the impact on fetal growth screening of existing national and international growth charts.
Study design: A questionnaire was sent to 14 Italian tertiary referral centers to explore biometric reference growth charts used in clinical practice. National and international (Intergrowth-21st and World Health Organization) fetal growth charts were tested on a large national cohort of low risk women with singleton uneventful pregnancy derived from a retrospective cross-sectional multicenter study (21 centers). The percentage of fetuses with biometric measurements below and above the 10th and 90th percentile for each biometric parameter and gestational week were calculated for each growth chart. The percentile curves of the study population were calculated by non-linear quantile regressions.
Results: Twelve Italian centers (86 %) answered to the questionnaire showing a wide discrepancy in the use of growth charts for fetal biometry. The cohort included 7347 pregnant women. By applying Intergrowth-21st growth charts the percentage of fetuses with head circumference, abdominal circumference and femur length below the 10th centile was 3.9 %, 3.6 % and 2.3 %, and above the 90th centile 29.9 %, 32.5 % and 46 %, respectively. The percentages for the World Health Organization growth charts for head and abdominal circumferences and femur length were: below the 10th centile 6.3 %, 7.2 % and 5.3 %, and above 90th centile 22.8 %, 21.3 % and 31.9 %, respectively.
Conclusions: The wide discrepancy in clinical use of fetal growth charts in Italian centers warrants the adoption of an uniform set of charts. Our data suggest that immediate application into clinical practice of international growth charts might result into an under-diagnosis of small for gestational age fetuses and, especially, in an over-diagnosis of large for gestational age fetuses with major consequences for clinical

Abbreviations: AC, Abdominal circumference; BMI, Body mass index; BPD, Biparietal diameter; EFW, Estimated fetal weight; FL, Femur length; HC, Head circumference; IG-21st, Intergrowth 21st; SD, Standard deviation; WHO, World Health Organization.

* Corresponding author at: Tamara Stampalija Fetal Medicine and Prenatal Diagnosis Unit, Institute for maternal and child health IRCCS Burlo Garofolo, University of Trieste, Via dell'Istria 65, 34100 Trieste, Italy.
E-mail addresses: Tamara.stampalija@burlo.trieste.it, tstampalija@units.it
(tullio.ghi@unipr.it (T. Ghi), valentina.rosolen@burlo.trieste.it (V. Rosolen), giuseppe.rizzo@uniroma2.it (G. Rizzo), enrico.ferrazzi@unimi.it (E.M. Ferrazzi), federico.prefumo@gmail.com (F. Prefumo), andrea.dallasta1@gmail.com (A. Dall'Asta), mariachiara.quadrifoglio@burlo.trieste.it (M. Quadrifoglio), tullia.todros@unito.it (T. Todros), fruscatiziana@gmail.com (T. Frusca).

[1] SIEOG working group on fetal biometric charts; collaborating authors are listed at the end of the article.

practice. On these grounds, there is an urgent need for a nationwide study for the prospective evaluation of international growth charts and, if needed, the construction and adoption of methodologically robust national growth charts.

Introduction

There is an ongoing international discussion regarding which fetal growth charts should be used [1]. As a matter of fact, an extensive and clinically significant variability among different growth charts has been proved, even between studies of the highest methodological quality [2]. Methodological aspects such as the study population, data collection, curve modeling and others are of crucial importance for the final outcome of the process [2]. Beside the methodological issues, there is also an ongoing discussion regarding whether one international standard might be adequate to assess fetal growth all around the globe, or are there some differences related to ethnicity supporting the adoption of growth charts constructed based on national data, or even the customization.

Recently, the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) Practice Guidelines on Ultrasound Assessment of Fetal Biometry and Growth [3] recommended the application of "*prescriptive biometry charts, obtained prospectively, truly population-based and derived from studies with the lowest possible methodological bias*", and called for the practitioners' awareness regarding national or even local growth charts. Such awareness requires an exploratory and preliminary analysis of the impact of different charts by applying reference values to local findings [3].

In Italy there is currently no chart recommended at a national level. In the past, two multicentric groups have produced two national growth charts, Nicolini et al. in 1986 [4] and Paladini et al. in 2005 [5]. Both growth charts were constructed on prospectively collected data in low-risk populations, but none completely fulfilled the ISUOG criteria and none provided a reference for the estimated fetal weight (EFW). More recently, customized fetal growth reference charts for parent's characteristics, race and parity have been published [6].

The aims of the study were to assess at a national level: 1) the use of biometric growth charts in clinical practice; 2) the validity of currently used non-customized national growth charts; and 3) the impact on fetal growth screening of new international charts proposed by the INTERGROWTH-21st (IG-21st) [7] and by the World Health Organization (WHO) [8] working groups.

Material and methods

Survey on fetal growth charts use

In order to investigate which fetal growth charts are in use at national level, a survey was performed involving 14 Italian tertiary referral centers. A short questionnaire was prepared to explore the biometric and Doppler charts used in clinical practice. The questionnaire was e-mailed to the lead of each Unit. In the case of no response, up to two e-mail reminders were sent at three-week intervals. Frequency and percentage distribution of adopted fetal growth charts were analyzed.

Comparison of national and international fetal growth charts

Fetal growth charts examined

The Nicolini growth charts were the result of a prospective cross-sectional multicentric (n = 8) study conducted in Northern Italy in the years 1984–1985 on uncomplicated pregnancies (n = 1426) [4]. The standardization was performed together with the evaluation of intra- and inter-observer reproducibility. Reference ranges from 12 to 41 gestational weeks for biparietal diameter (BPD), head circumference (HC) and abdominal circumference (AC) were calculated.

The Paladini growth charts were based on a prospective cross-sectional study conducted in three referral centers for prenatal diagnosis on 626 fetuses in early 2000ies [5]. Exclusion criteria were applied for all maternal and/or fetal conditions that could possibly affect fetal growth. Reference ranges from 16 to 40 weeks of gestation were computed for BPD, HC, AC, femur (FL), tibia, humerus, ulna and radius length.

The IG-21st prescriptive standards were derived from an international prospective longitudinal multicentric multiethnic study (8 countries) on 4321 pregnancies in years 2009–2014 [7]. Strict selection criteria were applied in order to include only low-risk pregnancies of healthy and well-nourished mothers from medium-high socioeconomic status [9]. Strict methodological criteria were applied for the biometric measurements that were blinded. Growth standards from 14 to 40 weeks of gestation were obtained for BPD, HC, AC, FL and EFW.

The WHO fetal growth charts are based on a prospective longitudinal multicentric multiethnic study on 1387 women conducted in 10 countries in years 2009–2014 [8]. Participants had no known health, environmental, nutritional or socio-economic constraints. Fetal, maternal and neonatal clinical conditions were retained, thus providing reference curves from 14 to 40 weeks of gestation for BPD, HC, AC, FL and EFW.

Study population

A cross-sectional retrospective multicentre study was conducted in 21 Italian referral Units, which had proven expertise in sonographic assessment of fetal growth and were opted in by the steering committee of this study. Data were derived from databases of each participating Unit concerning pregnancies delivered between January and September 2014. Details of the study were described elsewhere [6]. Uncomplicated singleton pregnancies delivered at 37–41 weeks with uneventful perinatal outcome and available information on parity, maternal height, weight and race were included. Pregnancies complicated by fetal structural or chromosomal anomalies, pre-existing maternal disease (such as hypertension, diabetes, renal and autoimmune disorders) or development of obstetrics complications (such as hypertensive disorders of pregnancy or gestational diabetes) were excluded. For the purpose of the present study, only mothers with a pre-pregnancy body mass index (BMI) in the range of 17–30 were selected. The pregnancies were dated based on first trimester ultrasound measurement of crown rump length. Sonographic measurements were obtained during routine screening ultrasound examinations, recommended at 19–21 and 30–34 weeks of gestation according to national guidelines [10]. A smaller number of fetal biometric data were collected out of the screening time interval when ultrasound was performed as a complement of clinical examination.

Sonographic measurements

Fetal measurements were made in accordance with the ISUOG guidelines [11] and as previously described [6]. The EFW (in grams) was computed using the Hadlock 3 formula [12]:

$[\log_{10}(EFW) = (1.326-(0.0000326*AC*FL)+(0.00107*HC)+(0.00438*AC)+(0.0158*FL)]$

Statistical analyses

The characteristics of the population were represented by median and interquartile range (IQR) or by frequency and percentage. The distribution of ultrasound scan occurrences per gestational age was graphically represented. We considered the BPD, AC and HC carried out between the weeks of gestation 14–40, while the FL and EFW were considered between the weeks of gestation 15–40 due to lack of measurements at 14 weeks. For each sonographic measurement and gestational week, the outliers were defined as minus or plus three times the standard deviation (SD) and therefore excluded from the statistical analyses.

In order to evaluate the clinical impact of the examined growth charts, we calculated for each biometric parameter and gestational week the percentage of fetuses whose biometric measurements were below and above the 10th and 90th percentile of each growth chart, respectively. Herein, we have included the percentages of the HC and AC parameters, since the HC represents an anthropometric measure and AC reflects mostly the nutritional fetal status. The percentages related to the BPD, FL and EFW measurements are represented in the Supporting Information.

Finally, quantile regressions were applied to the study population to estimate the predicted probability of each sonographic measurement by gestational week for the following percentiles: the 3rd, the 5th, the 10th, the 50th, the 90th, the 95th and the 97th percentiles (P3, P5, P10, P50, P90, P95 and P97, respectively). This was performed in order to be able to compare graphically the percentile curves of the study population with the growth charts assessed. Because the response functions BPD, HC, AC, FL and EFW were non-linear in parameters, non-linear quantile regressions were performed [13]. For BPD, HC, AC and FL the specification of the model formula is:

$$y \sim (\alpha + ß_1*(gw) + ß_2*(gw)^2 + ß_3*(gw)^3)$$

where y is one of the following sonographic measurements AC or FL or BPD or HC; gw is the gestational week of the sonographic measurements; α is the intercept; $ß_1$, $ß_2$ and $ß_3$ are the beta coefficients of the models.

For EFW the regression B-spline, with 4 knots, was applied to the non-linear quantile regression. [13] The specification of model formula is:

$$y \sim (\alpha + ß_1*(gw) + ß_2*(gw)^2 + ß_3*(gw)^3 + ß_4*(gw)^4)$$

where y is EFW; gw is the week of gestation at the time of EFW assessment; α is the intercept;

$ß_1$, $ß_2$, $ß_3$ and $ß_4$ are the beta coefficients of the model.

The observations of each sonographic measurement and the respective predicted probabilities were plotted to generate the curves based on the specified percentiles (P3, P5, P10, P50, P90, P95 and P97).

SAS (version 9.4 SAS Institute INC., Cary, N.C., USA), STATA (StataCorp. 2014. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) and quantreg and splines packages in R (version 3.5.2; R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/) softwares were used for the statistical analysis.

Ethical approval

The study was approved by the Institutional Review Boards of the participating Centres.

Results

Survey on fetal growth charts use

Twelve of the 14 referral centers answered the survey (86 %; Supporting Information S1). Fig. 1 shows wide discrepancies in the use of different fetal growth charts for biometric parameters among centers. Of note, half of the centers (n = 6) use Nicolini charts for BPD, HC and AC. [4] Nicolini charts do not provide references for LF and EFW, implying the need to use different charts for these parameters. The largest variability was hence observed for FL and EFW.

Comparison of national and international fetal growth charts

The sonographic measurements of 7347 pregnant women, who satisfied the inclusion and exclusion criteria, were considered for

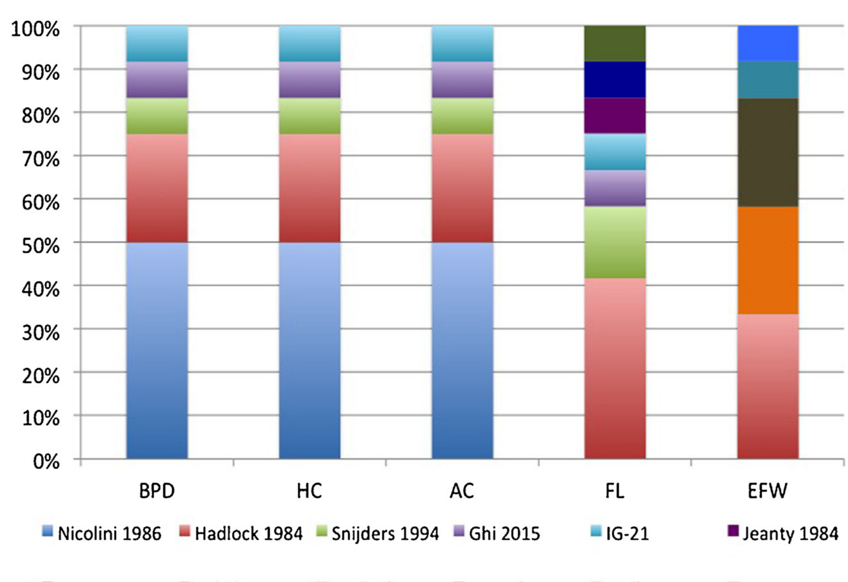

Fig. 1. Distribution of different fetal growth charts for biometric parameters among 12 Italian referral centers.

Table 1
Demographic and clinical characteristics of study population. IQR, interquartile range.

	N	Median (IQR) or N (%)
Caucasian of European ancestry (%)	7347	6475 (91.8)
Maternal height (cm)	7347	165 (9)
Pre-pregnancy weight (kg)	7347	58 (11)
Nulliparous n (%)	7345	4721 (64.3)
Gestational age at delivery (weeks)	7347	39 (2)
Newborn length (cm)	5546	50 (2)
Newborn weight (g)	7347	3300 (520)

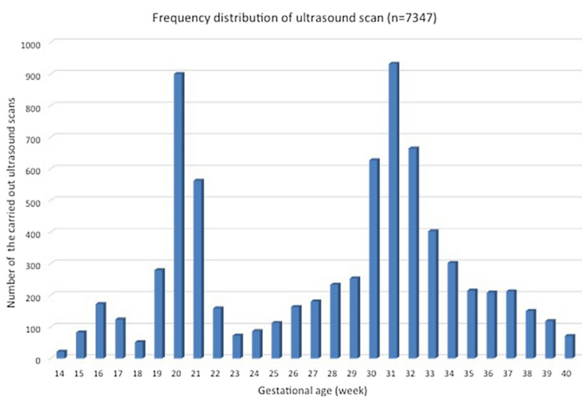

Fig. 2. Frequency distribution of carried out ultrasound scans.

this cross-sectional study. Table 1 shows the demographic and the clinical characteristics of mothers and newborns. The distribution of ultrasound scans according to gestational age is represented in Fig. 2.

Fig. 3 represents the 3rd, 5th, 10th, 90th, 95th and 97th percentiles of HC, AC, FL and EFW calculated on observed values, while BPD and numerical values are represented in Supporting Information (S2-S7). Of note, in our cohort the BPD was measured outer-to-inner, while the IG-21st methodology considered outer-to-outer measurement. [7] This might be a source of methodological bias and, thus, BPD was not further considered.

The percentages of fetuses with biometric measurements (HC and AC) below the 10th percentile and above the 90th percentile of each examined growth chart, for each gestational week, are shown in Tables 2 and 3. Tables for LF and EFW are shown in Supporting Information (S8-S9). Table 4 summarizes the proportion of all biometric measurements below the 10th and above the 90th percentile using each growth chart. Overall, the IG-21st growth charts identified the smallest proportion of fetuses below the 10th percentile and the largest proportion of fetuses above the 90th percentile, respectively. The proportion of fetuses with HC, AC and LF above the 90th centile was 29.9 %, 32.5 % and 46 %, respectively. While the WHO growth charts seem to be the closest to observed 10th percentile, the proportion of fetuses above the 90th percentile was also higher than expected for an appropriate distribution of percentiles, but smaller compared with the IG-21st growth charts: 22.8 %, 21.3 % and 31.9 % for HC, AC and LF, respectively. The comparisons between international growth charts and observed percentiles are shown in the Supporting Information (S10-S15).

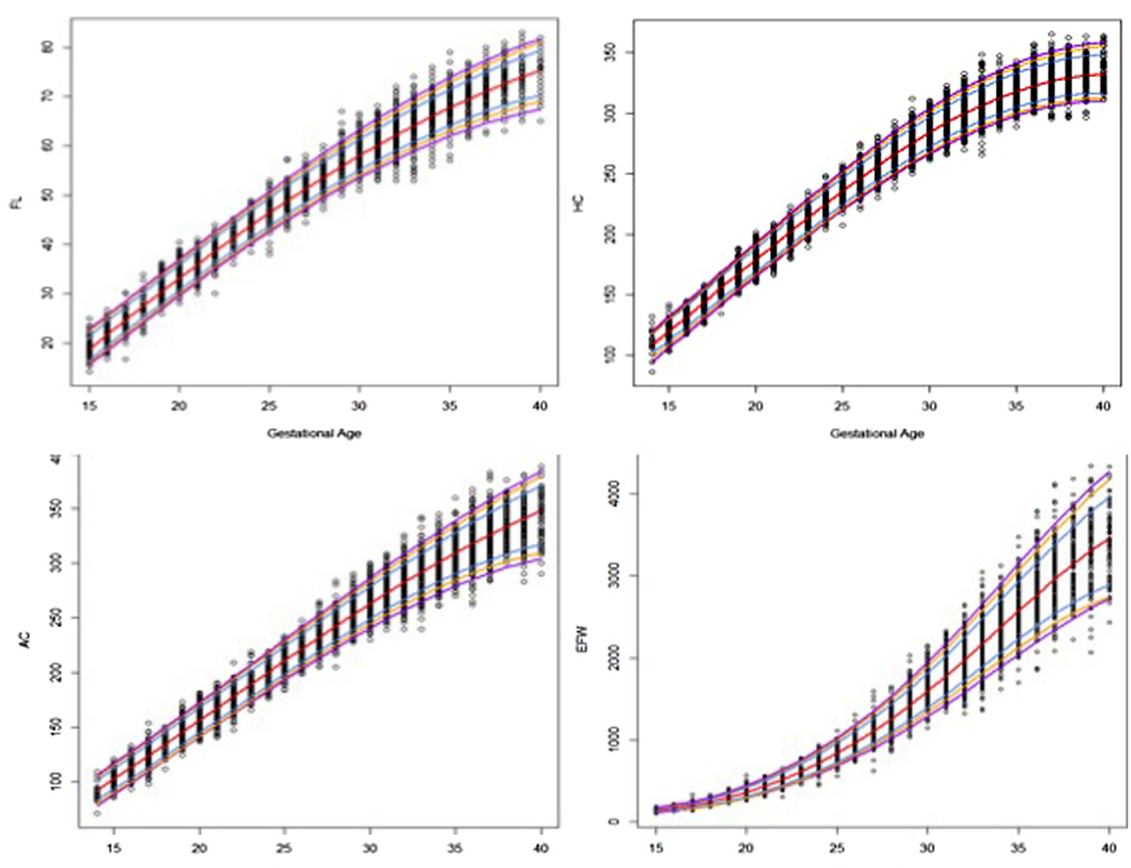

Fig. 3. The figure represents computed percentiles of fetal head circumference (HC), abdominal circumference (AC), femur length (FL) and estimated fetal weight (EFW) in the study population. See Supporting Information (S4-S7) for numerical values of each percentile.

Table 2
Percentage of fetuses with head circumference measurements below the 10th percentile and above the 90th percentile of considered fetal growth charts.

Gestational Age (week)	N	Intergrowth 21 Chart		WHO charts		Paladini charts		Nicolini charts	
		10^{th} pc	90^{th} pc	10^{th} pc	90^{th} pc	10^{th} pc	90^{th} pc	10^{th} pc	90^{th} pc
14	21	4.8	81.0	4.8	71.4			4.8	23.8
15	81	0.0	63.0	0.0	61.7			0.0	3.7
16	171	0.0	51.5	0.0	46.2			0.0	1.2
17	122	2.5	34.4	1.6	34.4	5.7	18.0	2.5	0.0
18	50	4.0	52.0	4.0	50.0	6.0	36.0	4.0	0.0
19	278	0.4	49.6	0.4	49.3	1.4	31.3	0.7	1.4
20	897	0.9	41.6	0.9	35.9	3.9	16.1	2.2	1.5
21	561	2.3	21.2	3.2	17.3	8.6	7.3	5.5	0.4
22	155	3.9	21.3	5.8	11.6	12.3	7.7	7.7	3.2
23	72	11.1	22.2	12.5	18.1	13.9	12.5	12.5	18.1
24	84	2.4	25.0	4.8	13.1	8.3	8.3	4.8	2.4
25	110	1.8	26.4	2.7	17.3	2.7	13.6	2.7	6.4
26	161	4.4	23.0	5.0	13.7	5.0	11.2	5.0	5.6
27	179	3.4	34.6	5.0	14.5	5.0	14.5	4.5	6.2
28	232	1.7	27.2	6.9	13.8	6.0	13.8	2.2	7.3
29	249	4.0	31.7	7.2	20.5	4.0	18.5	2.0	15.7
30	621	0.8	30.8	1.6	18.0	0.8	14.5	0.5	11.6
31	930	2.4	26.9	3.7	16.2	2.0	14.1	2.0	12.7
32	660	4.7	20.8	4.7	12.4	2.9	11.4	2.7	10.9
33	399	6.8	22.1	7.8	17.0	4.8	16.5	4.8	16.5
34	298	6.0	15.8	6.0	9.7	3.4	7.7	4.4	7.7
35	212	7.1	16.0	6.6	13.2	4.3	6.6	6.6	6.6
36	204	4.4	14.2	4.4	8.8	3.4	8.3	8.8	7.4
37	210	5.2	14.8	9.5	11.9	4.3	11.0	10.5	7.1
38	150	7.3	16.0	11.3	10.7	5.3	11.3	16.0	6.7
39	116	6.9	7.8	13.8	2.6	6.9	5.2	21.6	2.6
40	70	7.1	15.7	37.1	7.1	5.7	14.3	40.0	5.7

Discussion

Our study shows that there is a wide discrepancy among Italian referral centers regarding the fetal growth charts adopted for clinical purposes. This heterogeneity provides sufficient evidence to mandate actions in order to provide a recommendation by the Italian Society of Ultrasound in Obstetrics and Gynecology (SIEOG) regarding one set of fetal growth chart to be used nationally. For

Table 3
Percentage of fetuses with abdominal circumference measurements below the 10th percentile and above the 90th percentile of considered fetal growth charts.

Gestational Age (week)	N	INTERGROWTH-21 st Chart		WHO charts		Paladini charts		Nicolini charts	
		10^{th} pc	90^{th} pc	10^{th} pc	90^{th} pc	10^{th} pc	90^{th} pc	10^{th} pc	90^{th} pc
14	21	4.8	76.2	4.8	61.9			4.8	9.5
15	82	1.2	75.6	0.0	65.9			0.0	3.7
16	172	0.6	55.2	0.0	45.9			0.6	4.1
17	121	3.3	38.0	2.5	34.7	33.1	6.6	2.5	5.0
18	51	2.0	56.9	2.0	47.1	21.6	3.9	2.0	3.9
19	279	0.4	62.0	0.4	52.7	7.2	9.7	0.4	9.3
20	899	0.1	49.6	0.9	34.9	7.1	5.5	0.1	6.8
21	560	1.3	35.2	3.0	23.2	8.4	2.1	0.9	3.2
22	157	2.6	35.7	7.6	15.9	12.1	1.3	2.6	3.2
23	72	1.4	29.2	6.9	16.7	6.9	6.9	1.4	6.9
24	85	3.5	30.6	11.8	12.9	7.1	2.4	3.5	3.5
25	111	2.7	34.2	9.0	15.3	4.5	2.7	2.7	6.3
26	160	1.3	23.8	9.4	10.6	3.1	2.5	1.3	2.5
27	177	1.1	32.2	6.2	14.1	1.1	6.2	1.1	9.6
28	229	2.2	27.5	8.3	9.6	2.2	6.1	2.2	7.9
29	252	0.4	40.1	3.2	17.9	0.0	9.5	0.8	11.9
30	622	1.0	28.9	1.8	13.5	0.5	9.8	1.0	10.3
31	927	1.0	28.7	2.5	13.8	0.3	10.0	1.0	10.0
32	659	2.7	19.0	4.4	10.3	1.4	10.3	2.7	8.0
33	397	5.8	21.9	7.6	12.6	1.8	13.9	5.8	11.3
34	299	3.7	14.4	6.4	10.4	2.0	13.0	3.7	2.7
35	213	3.8	17.8	6.6	9.9	1.4	20.7	3.8	12.2
36	207	5.8	15.5	8.2	10.6	3.9	22.7	5.8	15.5
37	211	6.6	11.9	10.0	9.0	2.4	24.6	6.6	13.3
38	147	2.0	10.2	9.5	3.4	0.0	29.3	1.4	14.3
39	116	14.7	3.5	25.0	1.7	7.8	30.2	14.7	11.2
40	71	22.5	4.2	36.6	0.0	12.7	28.2	22.5	8.5

Table 4
Summary of percentages of 7347 pregnant women with fetal biometric measurements below the 10th centile or above the 90th centile using Intergrowth-21st, WHO, Paladini and Nicolini charts, respectively.

	<10th pc (%)				>90th pc (%)			
	IG-21	WHO	Paladini	Nicolini	IG-21	WHO	Paladini	Nicolini
HC	3.9	6.3	5.2	6.6	29.9	22.8	13.7	7.1
AC	3.6	7.2	6.2	3.5	32.5	21.3	11.6	7.9
LF	2.3	5.3	3.7	/	46	31.9	20.8	/
EFW	5.3	5.9	/	/	25.5	23.7	/	/

that reason an exploratory evaluation of the most commonly used national and international fetal growth charts was undertaken. The comparison of IG-21st [7], WHO [8], Paladini [5] and Nicolini [4] growth charts in a large cohort of low-risk pregnant women with uneventful singleton pregnancy showed that the IG-21st growth charts tend to underestimate the proportion of fetuses with AC below the 10th centile, while both IG-21st and WHO growth charts tend to overestimate the proportion of fetuses above the 90th percentile, although the effect was the highest for the IG-21st growth charts.

The multicenter WHO Child Growth Standards were published in 2006 [14] based on the assumption that all children have the same growth under optimal nutritional and socio-economic conditions, regardless of their ethnic origin. On this basis, two multicentric multiethnic studies have been performed to provide in-utero growth charts [7,8]. In the IG-21st project very strict inclusion criteria were adopted, and the finding was that in an ideal condition of health, nourishment, socio-economic and environmental circumstances, all fetuses are of similar size, independently of ethnicity [7]. Thus, the consortium proposed prescriptive standards to be used globally. The recruitment criteria in WHO were similar, but retained fetal, maternal and neonatal clinical conditions [8]. The results provided by WHO consortium demonstrated significant differences in fetal growth among countries.

Certainly, the concept of "one size fits all" is appealing for many reasons: there are available more than 80 fetal biometric charts [15] and some are of questionable methodological quality; there is a global internationalization process resulting in multi-ethnic societies; and the definition of ethnicity sometimes might be complex as in case of intermarriage. Nevertheless, concerns have been raised both from a theoretical [16–18] and practical [17–22] point of view, calling for attention and more rigorous evaluation [23] before implementing new international growth standards into clinical practice. Similar objections were recently raised for international child growth standards, notwithstanding the fact that they are widely adopted [24–26].

When we applied the IG-21st growth charts to our national cohort the prevalence of large HC, AC and FL was two to three times higher than expected. These findings are in line with other reports from Norway [17], Netherlands [27], Greece [22] and France [20,28]. Opposite to these findings, the IG-21st growth charts yielded an over-estimation of small for gestational age fetuses in a Chinese cohort [16]. In a prospective study, the same group evaluated the EFW IG-21st and WHO growth charts in a Southern Chinese population and found significant differences when compared to local reference [19].

Reasons for these discordant findings might be the actual variability of population characteristics, and criteria of recruitment (ie population, prevalence of gestational diabetes, obesity, pre-pregnancy undernutrition, etc). However, studies that considered only low-risk population [17], similar to ours, and those that applied strict IG-21st criteria to replicate the sample over which the IG-21st growth charts were computed [17,20], found similar differences in fetal growth, as such not explainable by "risk factors". Moreover, the strict application of IG-21st criteria excluded 70–80 % of pregnant women both in Scandinavian and French settings, questioning the applicability of these growth charts [17,20]. Finally, the evolution in ultrasound imaging technology might account for some of the differences in charts built before or after the mid-2000′s, but this has been proved for FL measurements only [29].

Overall, these data suggest that there might be differences linked to ethnic origin and not fully explained by maternal, socio-economic or other methodological factors [2] as already suggested by the NICHD [30] and WHO [8] groups. For these reasons, some countries have not justified the change from local national or regional growth charts to international standards [17,18,27].

The strength of our study is that it was based on a large sample of ultrasound measurements obtained from a cohort of pregnant women that are representative of all areas of our country. Although this low-risk population did not completely fulfill the IG-21st selection criteria, all pregnancies had uneventful obstetric and neonatal outcome, including appropriate for gestational age birthweight. Mothers had normal pre-pregnancy BMI, were free from pre-pregnancy and/or antenatal diseases. Pregnancies obtained by assisted reproductive technology were not excluded. The limitation is that this was a historical cohort from routine clinical examinations. Thus, there was no research protocol, and training, blinding and quality control were not performed. However, the measurements were performed by experienced physicians according to ISUOG guidelines, in a setting that truly reflects common clinical practice. Another limitation is that the vast majority of measurements were performed at 20 and 30 weeks of gestation, as suggested by national screening protocols, making other gestational periods less represented.

Conclusion

Our data suggest that, despite indisputable advantages that international growth standards might offer, immediate application into clinical practice might result into an under-diagnosis of small for gestational age fetuses and, especially, in an over-diagnosis of large for gestational age fetuses with major consequences for clinical practice. On the other hand, existing national growth reference charts lack crucial biometric parameters and centiles (EFW for Paladini, FL and EFW for Nicolini and 3rd and 97th centiles are not reported for both). This is of major importance, if we consider that recent consensus criteria suggested AC and EFW below the 3rd centile as independent criteria for the diagnosis fetal growth restriction [31]. Whether the differences observed have any clinically meaningful effect on the prevention of adverse pregnancy outcomes, remains to be determined. On these grounds, there is an urgent need for a nationwide study for the prospective evaluation of international growth charts and, if needed, the construction of methodologically robust national growth charts.

SIEOG working group on fetal biometric charts collaborating authors

G. Altobelli, M. Arduini, E. Bertucci, S. Boito, G. Canzone, A. Capece, E. Carboni, E. Cariati, L. Cariello, I. Cetin, N. Chianchiano, G. Clerici, E. Cosmi, V. D'Addario, D. DiMartino, E. Cosmi, R Giacchello, A. Giancotti, M. Giorgina, A. Maiandi, L. Mandia, G.M. Maruotti, A. Mazzocco, F. Mecacci, L. Nicoletti, L. Pasquini, E. Periti, N. Persico, L. Rizzo, A. Rossi, A. Tenore, P. Vergani, C. Verrotti, E. Viora, S. Visentin, P. Volpe, and C. Zanardini.

Funding information

No funding was obtained for this study.

Declaration of Competing Interest

The authors state no conflict of interest.

References

[1] Thilaganathan B. Ultrasound fetal weight estimation at term may do more harm than good. Ultrasound Obstet Gynecol 2018;52(1):5–8.
[2] Ioannou C, Talbot K, Ohuma E, et al. Systematic review of methodology used in ultrasound studies aimed at creating charts of fetal size. BJOG 2012;119(12) 142-39.
[3] Salomon LJ, Alfirevic Z, Da Silva Costa F, et al. ISUOG Practice Guidelines: ultrasound assessment of fetal biometry and growth. Ultrasound Obstet Gynecol 2019;53(6):715–23.
[4] Nicolini U, Todros T, Ferrazzi E, et al. Transverse fetal growth curves. A multicenter study. Minerva Ginecol 1986;38(11):873–87.
[5] Paladini D, Rustico M, Viora E, et al. Fetal size charts for the Italian population. Normative curves of head, abdomen and long bones. Prenat Diagn 2005;25 (6):456–64.
[6] Ghi T, Cariello L, Rizzo L, et al. Società Italiana di Ecografia Ostetrica e Ginecologica Working Group on Fetal Biometric Charts. Customized Fetal Growth Charts for Parents' Characteristics, Race, and Parity by Quantile Regression Analysis: A Cross-sectional Multicenter Italian Study. J Ultrasound Med 2016;35(1):83–92.
[7] Papageorghiou AT, Ohuma EO. Altman DG et al; International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st). International standards for fetal growth based on serial ultrasound measurements: the Fetal Growth Longitudinal Study of the INTERGROWTH-21st Project. Lancet 2014;384(9946)869–79 6.
[8] Kiserud T, Piaggio G, Carroli G, et al. The world health organization fetal growth charts: a multinational longitudinal study of ultrasound biometric measurements and estimated fetal weight. PLoS Med 2017;14(1 January)e1002220 24.
[9] Villar J, Altman DG, Purwar M, et al. International fetal and newborn growth consortium for the 21st century. The objectives, design and implementation of the INTERGROWTH-21st project. BJOG 2013;120(Suppl 2):9–26.
[10] Linee Guida Gravidanza Fisiologica. Linea Guida 20. Ministero della salute. 2011. . Accessed on October 2019 http://www.salute.gov.it/imgs/C_17_pubblicazioni_1436_allegato.pdf.
[11] Salomon LJ, Alfirevic Z, Berghella V, et al. ISUOG Clinical Standards Committee. Practice guidelines for performance of the routine mid-trimester fetal ultrasound scan. Ultrasound Obstet Gynecol 2011;37(1):116–26.
[12] Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body, and femur measurements: a prospective study. Am J Obstet Gynecol 1985;151:333–7.
[13] Koenker R. Quantile regression in R: a vignette. 2018. . Accessed on September 2011 https://cran.r-project.org.
[14] WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards based on length/height, weight and age. Acta Paediatr Suppl 2006;450(April):76–85.
[15] Ioannou C, Talbot K, Ohuma E, et al. Systematic review of methodology used in ultrasound studies aimed at creating charts of fetal size. BJOG 2012;119 (12):1425–39.
[16] Kramer MS. Foetal growth standards: description, prescription, or prediction? Paediatr Perinatl Epidemiol 2019;33:57–8.
[17] Sletner L, Kiserud T, Vangen S, Nakstad B, Jenum AK. Effects of applying universal fetal growth standards in a Scandinavian multi-ethnic population. Acta Obstet Gynecol Scand 2018;97(2):168–79.
[18] Cheng Y, Leung TY, Lao T, Chan YM, Sahota DS. Impact of replacing Chinese ethnicity-specific fetal biometry charts with the INTERGROWTH-21(st) standard. BJOG 2016;123(Suppl 3):48–55.
[19] Cheng YKY, Lu J, Leung TY, Chan YM, Sahota DS. Prospective assessment of INTERGROWTH-21st and World Health Organization estimated fetal weight reference curves. Ultrasound Obstet Gynecol 2018;51(6):792–8.
[20] Heude B, Le Guern M, Forhan A, et al. Are selection criteria for healthy pregnancies responsible for the gap between fetal growth in the French national Elfe birth cohort and the Intergrowth-21st fetal growth standards? Paediatr Perinat Epidemiol 2019;33(1):47–56.
[21] Liu S, Metcalfe A, León JA, Sauve R, Kramer MS, Joseph KS. Canadian perinatal surveillance system (Public health agency of canada). Evaluation of the INTERGROWTH-21st project newborn standard for use in Canada. PLoS One 2017;12(3)e0172910 3.
[22] Sotiriadis A, Eleftheriades M, Chatzinikolaou F, Hassiakos D, Chrousos GP, Pervanidou P. National curves of foetal growth in singleton foetuses of Greek origin. Eur J Clin Invest 2016;46(5):425–33.
[23] Zeitlin J, Vayssière C, Ego A, Goffinet F. More validation is needed before widespread adoption of INTERGROWTH-21st fetal growth reference standards in France. Ultrasound Obstet Gynecol 2017;49(4):547–8.
[24] Júlíusson PB, Roelants M, Hoppenbrouwers K, Hauspie R, Bjerknes R. Growth of Belgian and Norwegian children compared to the WHO growth standards: prevalence below -2 and above +2 SD and the effect of breastfeeding. Arch Dis Child 2011;96(10):916–21.
[25] Christesen HT, Pedersen BT, Pournara E, Petit IO, Júlíusson PB. Short stature: comparison of WHO and national growth Standards/References for height. PLoS One 2016;11(6):e0157277.
[26] Natale V, Rajagopalan A. Worldwide variation in human growth and the World Health Organization growth standards: a systematic review. BMJ Open 2014;4 (1):e003735.
[27] van de Kamp K, Pajkrt E, Zwinderman AH, van der Post JA, Snijders RJM. Validation of reference charts for mid-trimester fetal biometry. Fetal Diagn Ther 2019;45(1):42–9.
[28] Stirnemann JJ, Fries N, Bessis R, Fontanges M, Mangione R, Salomon LJ. Implementing the INTERGROWTH-21st fetal growth standards in France: a' flash study' of the College Français d'Echographie Foetale (CFEF). Ultrasound Obstet Gynecol 2017;49(4):487–92.
[29] Økland I, Bjåstad TG, Johansen TF, Gjessing HK, Grøttum P, Eik-Nes SH. Narrowed beam width in newer ultrasound machines shortens measurements in the lateral direction: fetal measurement charts may be obsolete. Ultrasound Obstet Gynecol 2011;38:82–7.
[30] Buck Louis GM, Grewal J, Albert PS, et al. Racial/ethnic standards for fetal growth: the NICHD fetal growth studies. Am J Obstet Gynecol 2015;213(4) 449.e1-449.e41.
[31] Gordijn SJ, Beune IM, Thilaganathan B, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol 2016;48 (3):333–9.