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Optimal Standards for Fetal Biometry: To Each Measurement Its Fitting Model

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Key Words
Abdominal circumference · Femur length · Fetal growth · Head circumference · Mathematical model · Ultrasonography

Abstract
Objective: To determine the best mathematical model to construct charts of fetal abdominal circumference (AC) and femur length (FL). ***Methods:*** Ultrasound measurements were made on 1,336 normal fetuses in one center. Four mathematical models were compared (a linear-quadratic model, a linear-cubic model, the Rossavik model and a new two-phase model, which has been found to best fit fetal head data). ***Results:*** The best fitting of AC and FL data was obtained with the linear-quadratic model without separate computing for gender. Centile charts have been computed. ***Conclusion:*** Fetal growth of AC and FL is much simpler than that of the head. Therefore, a unique mathematical model should not be used to fit all measurements.

Introduction

In clinical practice, the diagnosis of growth impairment is largely dependent on the accuracy of the charts used. Most of these standards have been computed from cross-sectional data sets, and one of the most important steps to compute these standards concern the choice of the model for data computation. Numerous models, mostly polynomials, have been proposed to fit cross-sectional data, and appropriate methodologies have been recommended to construct charts of fetal size from these models [1, 2]. In a previous study [3], we attempted to determine the best model describing the kinetics of fetal head growth. We found a new two-phase mathematical model, computed independently for male and female data, taking into account the increasing inter-subject variability with gestational age, and the decrease in mean growth rate at about 30 gestational weeks, which has been reported previously [4]. The present study extends the previous model on two other dimensions usually involved in routine ultrasound screening of fetuses: the abdominal circumference (AC) and femur length (FL). Therefore, cross-sectional data were computed and tested for AC and FL using four fitting models (a model previously fitted to the head variable and three other current mathematical models: a linear-quadratic model, a linear-cubic model and the Rossavik model [5]). The aim of this study was to determine the best fitting models for FL and AC, and thus to build accurate centile charts.

Subjects and Methods

Subjects
This study included 1,336 subjects (684 males and 652 females) born between 1995 and 1997 at the Regional Maternity of Nancy (France). They ranged in age from 12 to 38 gestational weeks (table 1). Gestational age (in completed weeks) was determined from the date of the last menstrual period and confirmed at the first ultrasound examination.

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Table 1. Sample sizes (n), means (μ) and standard deviations (σ) in FL and AC according to gestational age (GA)

GA weeks	FL males n	FL males μ ± σ, mm	FL females n	FL females μ ± σ, mm	p value	AC males n	AC males μ ± σ, mm	AC females n	AC females μ ± σ, mm	p value
12	19	9.0±2.6	14	8.8±0.9	NS	22	59.5±6.0	18	59.2±4.5	NS
13	30	11.5±1.9	27	11.7±1.7	NS	27	71.3±8.1	25	71.1±7.3	NS
14	23	13.9±2.2	31	15.2±1.5	<0.05	21	85.7±8.0	30	80.8±6.1	NS
15	26	17.8±1.8	14	19.1±1.8	<0.05	21	95.6±8.7	13	91.7±10.3	NS
16	27	22.1±1.8	17	21.1±2.1	NS	24	109.3±8.6	12	105.8±4.5	NS
17	21	24.8±1.8	20	24.8±2.1	NS	13	126.1±8.0	18	123.4±10.2	NS
18	20	27.8±1.9	16	28.6±2.3	NS	17	130.8±8.6	14	132.8±9.5	NS
19	11	30.6±2.1	16	31.4±1.7	NS	11	143.5±9.6	14	143.3±7.3	NS
20	26	33.7±1.7	14	34.1±1.5	NS	24	154.5±8.5	14	156.6±6.4	NS
21	20	36.8±2.6	17	36.3±2.1	NS	18	169.5±7.8	15	163.6±10.7	NS
22	27	39.2±1.5	27	39.1±1.4	NS	27	176.8±7.9	22	176.4±9.9	NS
23	33	42.1±1.4	42	42.4±1.8	NS	32	190.3±9.1	37	183.7±10.8	<0.01
24	28	44.2±2.1	41	45.0±2.3	NS	26	199.1±11.9	35	200.7±12.8	NS
25	32	47.2±2.1	25	46.4±2.5	NS	29	207.6±10.0	23	205.3±10.4	NS
26	26	48.5±2.2	24	48.8±2.4	NS	25	219.8±9.7	24	210.4±12.3	<0.01
27	25	50.3±2.0	17	52.3±2.4	<0.01	22	223.7±9.8	13	222.5±7.1	NS
28	18	54.0±1.6	17	53.4±2.4	NS	14	237.8±13.7	14	233.4±10.1	NS
29	24	56.2±2.2	17	56.4±2.2	NS	21	246.8±12.9	15	248.6±12.3	NS
30	24	57.7±2.1	13	57.8±2.4	NS	25	256.7±11.9	11	248.6±14.0	NS
31	18	59.7±2.9	24	60.7±2.1	NS	15	266.1±9.8	23	265.1±12.4	NS
32	32	62.5±2.5	31	62.7±2.1	NS	30	277.7±15.4	30	273.1±10.1	NS
33	37	65.1±2.1	41	64.1±2.9	NS	31	289.3±15.0	37	280.9±18.0	<0.05
34	35	67.0±2.4	38	66.5±2.6	NS	33	303.6±15.6	36	292.7±13.0	<0.01
35	30	68.1±2.8	31	67.5±2.1	NS	28	309.2±18.8	29	301.4±16.1	NS
36	18	70.7±3.2	25	69.8±5.3	NS	15	317.7±19.6	24	307.3±19.8	NS
37	22	70.9±2.7	21	70.6±2.3	NS	22	325.4±17.7	19	318.9±16.3	NS
38	12	72.6±2.8	7	72.4±4.9	NS	13	317.5±20.9	7	327.7±24.0	NS

Student's test was performed to compare mean values between males and females. NS = Nonsignificant.

All scans were performed for the routine screening perinatal program of all pregnancies and were not clinically indicated. Fetuses with malformations and premature babies were excluded retrospectively from the study. Multiple pregnancies and pathological pregnancies (including maternal diabetes, maternal hypertension and severe infections) were also excluded. Due to the maternity program of ultrasound examinations (at determined gestational weeks), the distribution of cases was uneven throughout the gestation.

Measurements

Each fetus was included only once in the study (cross-sectional data). Therefore, only one ultrasound examination was selected at random among the several examinations performed on each fetus during pregnancy.

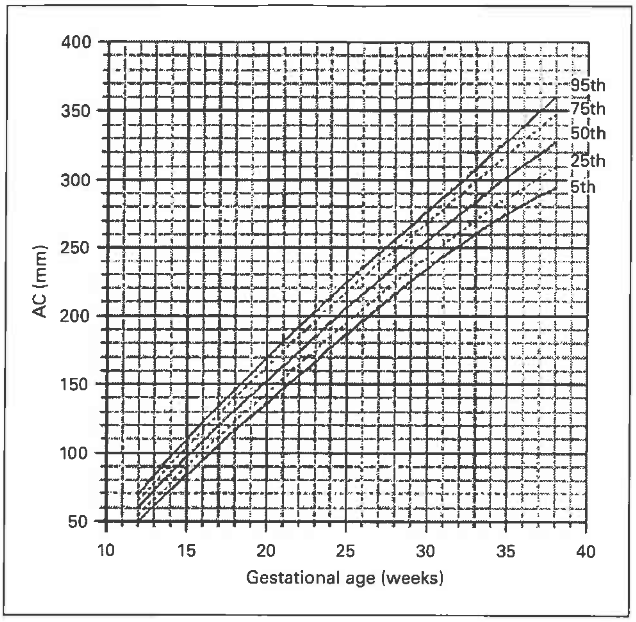
Scans were made by three experienced operators, using sonographers Toshiba SSH 140A and SSA 250A (Tokyo, Japan). Measurements were made according to the rules defined by Hadlock et al. [6]. The AC was measured on a transaxial plane showing the umbilical portion of the left portal vein (portal sinus) and the adrenal glands by electronic determination of the ellipse circumference. The femur was measured along the long axis of the diaphysis, when the femur is horizontally positioned.

Mathematical and Statistical Analysis

In order to determine if separate modeling of male and female data was required, we tested gender differences. Gender differences in AC and FL means were significant in a few age intervals (table 1). However, variance analysis performed in the whole gestational period showed no significant gender differences in AC ($p = 0.83$) as well as in FL ($p = 0.18$). Consequently, we did not compute distinct models for males and females.

Four fitting models were computed and tested in this study. The first one was developed by Pineau [7], and successfully tested on head circumference (HC) and biparietal diameter data [1]. Three other commonly used models were also computed: a linear-quadratic model ($a + bt + ct^2$), a linear-cubic model corresponding to the model used by Deter et al. [8] to fit longitudinal data ($a + bt + ct^3$) and the Rossavik equation [4].

To test the four models, we utilized the SYSTAT software to calculate the coefficient of determination (R^2) and the standard error of estimate [$SEE = \sigma\sqrt{(1 - R^2)}$].



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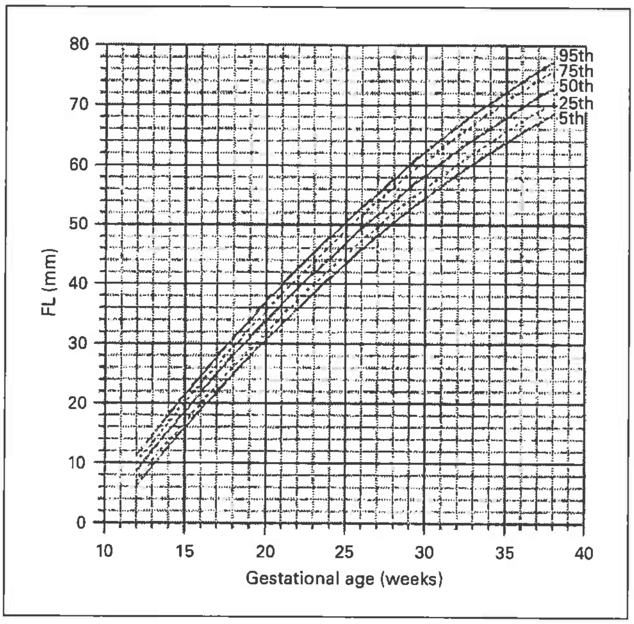

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Table 2. Accuracy of four mathematical models applied to AC and FL data

	a	γ	b	R^2, %	SEE
Pineau's model [3]: $a \cdot t^{\gamma} + b \cdot dy/y^{\alpha} = k \cdot dt/t^{\beta}$					
AC	100.4	0.50	−293.1	99.87	2.99
FL	252.1	0.15	−357.5	99.93	0.47
Linear-quadratic model: $a + b \cdot t + c \cdot t^2$					
AC	−102.60	14.53	−0.08	99.91	2.53
FL	−38.10	4.33	−0.04	99.96	0.39
Linear-cubic model [8]: $a + b \cdot t + c \cdot t^3$					
AC	−87.98	12.53	0.001	99.90	2.61
FL	−31.71	3.45	−0.0005	99.94	0.45
Rossavik model [5]: $c \cdot t^{(k + st)}$					
AC	0.235	2.36	−0.01	99.68	4.65
FL	0.0025	3.56	−0.02	99.15	1.85

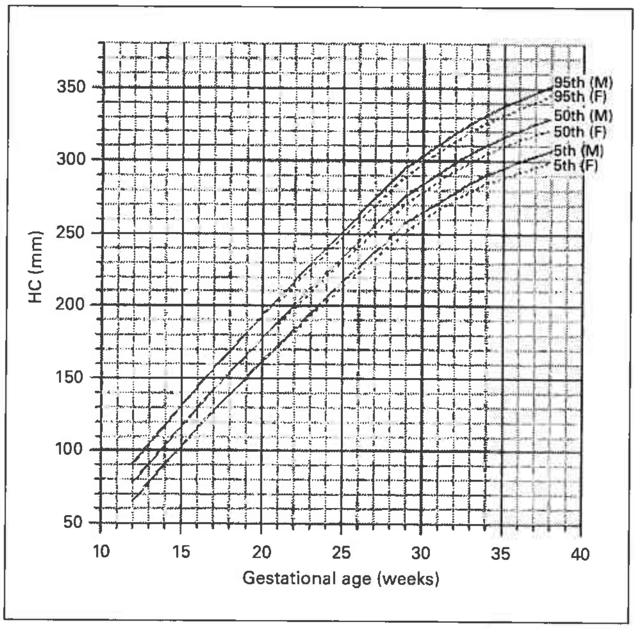

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Fig. 1–3. Growth charts of AC (**1**), FL (**2**) and HC (**3**) in relation to gestational age. F = Females; M = males.

Results

The constants, R^2 and SEE, for each mathematical model fitted to the AC and FL mean data are reported in table 2. All models fitting AC and FL data have high values of R^2 ($R^2 \geq 99.9$). Nevertheless, differences in SEE exist between the four models:

For AC, the biggest SEE, indicating the least accurate model, was found for the Rossavik equation (SEE = 4.65). The SEE for the three other models were closer to each other, varying from 2.53 to 2.99. The smallest SEE (2.53), and consequently the most accurate fit, corresponded to the linear-quadratic model. For FL, the same tendencies were observed. The least accurate model was the Rossavik equation (SEE = 1.85), the best one was the linear-quadratic model (SEE = 0.39).

Consequently, the linear-quadratic model was chosen to fit mean data of FL and AC. Percentiles were further computed from the fitted mean values and from the linear fitted standard deviations. Percentile curves for FL and AC are reported in figures 1 and 2. As a comparison, the percentile HC curves derived from a previous study of the same population using the same methodology [3] are reported in figure 3.

Discussion

In a previous study, we have shown that the commonly used simple models are not the most appropriate to describe the kinetics of fetal head growth. Biparietal and HC data were best fitted with a two-phase mathematical model, taking into account a modification of growth kinetics at 30 gestational weeks, and computed independently for males and females [3]. In this study, the same mathematical models were tested on AC and FL data. Unexpectedly, the best fitting was obtained with the simplest model: the linear-quadratic one. Furthermore, in contrast to HC, accurate modeling of FL and AC data did not require separate computing of data for males and females.

In the literature, the linear-quadratic model was not the most commonly used model for FL and AC data. AC data have previously been fitted by a linear-cubic model [9, 10], a logistic logarithmic function or an exponential power function [11], a locally weighted least square fit [12] and the simple linear-quadratic model [13].

Femur data have been fitted by a linear-cubic model [14], a locally weighted least square fit [12], as a function of tangens hyperbolicus [15] and using the linear-quadratic model [7].

Since we found distinct accurate models fitting different biometric measurements with the same methodology, it should be inferred that the kinetics of growth of these dimensions were different. The head appeared to have a more complex growth than AC and FL, since its kinetics is biphasic and gender dependent. This particular biphasic pattern of growth is partly related to the particularity of human brain development or to the fetal rotation in the maternal uterus in the second half of gestation, modifying the stress on the fetal head. However, this hypothesis does not explain the gender differences in HC.

Finally, as announced in a previous study [3], accurate new standards of AC, FL and HC, useful for routine fetal screening, have been computed, and corresponding centile charts given. The next step could be to evaluate these curves for the diagnosis of small-for-gestational-age or macrosomic fetuses.

A practical conclusion of this study is that a unique fitting model should not be used for all fetal biometric measurements. Mathematical models used to describe the growth of each dimension should be carefully chosen as close as possible to the raw data. This consideration is also relevant for 'individualized growth charts'.

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