Virchows Archiv (2019) 475:499–511
https://doi.org/10.1007/s00428-019-02639-0

ORIGINAL ARTICLE

# Fetal autopsy parameters standards: biometry, organ weights, and long bone lengths

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Received: 2 December 2018 / Revised: 12 July 2019 / Accepted: 30 July 2019 / Published online: 16 August 2019


## Abstract

Fetal and perinatal growth charts and tables are essential for proper interpretation of autopsy anthropometric parameters. These parameters depend on factors that may vary between populations; thus, it is recommended that standards be developed from local target populations to ensure that they are truly representative. In this study, we established standards for a complete set of autopsy fetal parameters, including biometrical measurements, organ weights and long bone lengths, based on autopsy data collected retrospectively from a sample of Portuguese fetuses and neonates. Using a robust statistical regression methodology, to fit mean and standard deviation models, we constructed growth curves for gestational ages between 12 and 42 weeks, which aim to be useful for autopsy examination, particularly in the Portuguese population.

**Keywords** Fetal biometry · Organ weights · Portuguese · Autopsy · Reference values

## Introduction

Autopsy is an important tool in fetal and perinatal pathology. It allows not only to define the cause of death but also to characterize developmental fetal anomalies and malformations, evaluate maturation and growth, and determine gestational age and intrauterine retention time after fetal death.

Fetal development is characterized by growth and maturation of tissues and organs that follows recognized rates and patterns. Indeed, standard growth curves and tables have been established based on datasets of fetal and neonatal autopsies.[1–13] These standards have become essential for the correct evaluation of fetal and perinatal pathology during autopsy examination. The careful evaluation of anthropometric parameters, such as biometric measurements, organ weights and long bone lengths, followed by their interpretation compared to reference curves and tables, secures the diagnosis of growth and development alterations.

Previous studies aiming to establish autopsy parameter standards have, however, varied designs, encompassing different gestational age periods, different exclusion criteria, and different parameter datasets.[1–13] Additionally, some were developed prior to the widespread use and improvements of ultrasound and use different definitions of gestational age.[1–5] Importantly, the various studies derive from different

This article is part of the Topical Collection on *Quality in Pathology*

**Electronic supplementary material** The online version of this article (https://doi.org/10.1007/s00428-019-02639-0) contains supplementary material, which is available to authorized users.

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populations. It is known that anthropometric parameters depend on factors that may vary between populations, such as race and ethnicity, socioeconomic status, health care, diet, lifestyle, geographic place of birth, and altitude. In 2006, Archie et al. compiled data and created regressions from multiple sources both to increase accuracy and to condense available data into a single standard, providing robust external standards.[10] Yet, these and other authors claim that internal standards should be developed from local populations to ensure that they are truly representative.[9, 11, 13] Only this way can a fetus be compared to others in the same population, examined with the same procedures, and following consistent clinical definitions.

For the Portuguese population, no study has yet established complete fetal anthropometric standards to be used in autopsy examination. Thus, we aimed to construct growth curves and tables representative of our local population, encompassing the complete set of parameters used in fetal autopsy examination, namely, biometric measurements, organ weights, and long bone lengths for all gestational ages between 12 and 42 weeks.

## Methods

This study was conducted at the Centro Hospitalar S. João in Porto, Portugal, after being approved by the hospital's ethics committee (CES 334.15). Data was retrospectively collected from the records of 1062 consecutive fetal and perinatal autopsies performed at the Developmental and Perinatal Unit of the Pathology Department between 2006 and 2015. All autopsies were performed by a fully dedicated team, including a pathologist and two technicians with special training, using the same standard procedures, which included the measurement of biometrical parameters, organ weights, ratios and long bone lengths.[14–16]

Biometrical parameters (Fig. 1) encompassed body weight (BW), crown-heel length (CHL), crown-rump length (CRL), head circumference (HC), chest circumference (CC), abdominal circumference (AC), hand length (HL), foot length (FL), inner canthal distance (ICD), outer canthal distance (OCD), philtrum length (PL), and internipple distance (IND). Organ weights, namely thymus, heart, lungs, liver, spleen, kidneys, and adrenals, were evaluated after in situ fixation (following adequate body cavity opening) for most fetuses under 24 weeks, and in fresh for fetuses older than 24 weeks of gestation. Exceptions included fetuses older than 24 weeks in the setting of medical termination of pregnancy or fetuses with a clinical suspicion of a complex malformation, for which evaluation was made after in situ fixation. Paired organs were weighed together. Brains were carefully removed and placed directly into a container containing the fixative (formol and 5% glacial acetic acid solution with NaCl addition) that was weighed in advance and immediately after, allowing an accurate measure of the entire brain weight in fresh. Long bone lengths (Fig. 2) were evaluated using Faxitron or conventional X-rays, as well as biparietal diameter (BPD) and fronto-occipital diameter (FOD). Data regarding maceration grade and cause of death were also collected, when applicable.

Gestational age was defined clinically, i.e., calculated in weeks from the beginning of the last menstrual period, adjusted by first-trimester ultrasound measurements, and confirmed by the estimation of organ maturation at autopsy.

We reviewed each autopsy report to determine its suitability for inclusion in this study. General exclusion criteria were (1) multiple gestation, (2) newborns > 24 h, (3) uncertain gestational age, (4) severe maceration, (5) chromosomal abnormalities, (6) intrauterine growth restriction, (7) severe septicemia and viral infections, (8) fetal hydrops, (9) skeletal dysplasia, and (10) fetuses from diabetic mothers. Considering these criteria, 644 autopsies were fully excluded from the study. Additionally, partial exclusion criteria were applied for fetuses with malformations and disruptive lesions. Namely, when a major malformation or a macroscopic disruptive lesion was identified and affected in isolation a specific parameter, that parameter was excluded but the remaining autopsy data was considered informative, and therefore, remained included in the study (supplementary table—Online Resource 1).

Data was tabulated in a spreadsheet and analyzed using STATA 13 (STATACorp, Texas, USA). Predictive mean and standard deviation (SD) models were established using the parametric method recommended by Altman and Chitty.[17, 18] In brief, the mean of each study parameter was modeled as a function of gestation age. Least-square regression analysis was done by testing linear, quadratic, cubic, quartic, logarithmic, and power models. For each study parameter, the choice of the adequate model was based on its statistical significance, high coefficient of determination, and the visual inspection of the goodness of fit. The same procedure was followed to model SD as a function of gestational age by using the absolute residuals between the observed values and the fitted mean curve. Next, the mean curve was refitted by using weights that take into account the variability of SD with gestational age. Considering the obtained fitted mean and SD models, we then calculated centiles using the formula: centile = mean + Z × SD, where $P$ is the corresponding centile value of the Gaussian distribution (e.g., for 3rd and 97th centiles Z equals ± 1.881, for 5th and 95th centiles Z equals ± 1.645, and for 10th and 90th centiles, Z equals ± 1.282). Charts were computed by plotting predicted means and 3th, 5th, 10th, 25th, 75th, 90th, 95th, and 97th centiles lines, some, superimposed to a scatter of observed parameters against gestational age.


**Fig. 1** Examples of fetal biometric measurements taken during autopsy examination. **a** Crown-heel length (CHL) is measured with the fetus placed on its back with spine and one limb straightened as much as possible. It can best be measured using a scale with a fixed upright at fetal head and a movable upright at the feet. When such scale is not available, crown-heel length can be measured improvising an upright for the head (by using a handle or a tweezer as shown), or a string, and read off against a ruler. **b** Crown-rump length (CRL) is measured with the fetus placed on its back with the hips flexed at 90 degrees and the spine straightened. CRL is approximately two thirds of the CHL. Considering this relation, a correction may be made to assess the expected length in malformations such as anencephaly. **c** Head (fronto-occipital) circumference is measured with a string and read off against a ruler. The string wraps around the widest possible circumference of the head, passing through the broadest part of the forehead above eyebrow, above the ears, and most prominent part of the back of the head. Head circumference and CRL do not differ by more than 1 cm. **d** Abdominal circumference is measured with a string and read off against a ruler. The string wraps around the abdomen near the border of the hepatic dullness, which, depending on gestational age, can be at the umbilicus (smaller fetuses) or above (older fetuses and neonates). **e** Foot length is defined by the distance from the tip of the great toe to the posterior surface of the heel. **f** Hand length is measured from the tip of the third finger to the end of the palm at the first crease of the fist

## Results

### Study population

Of the 1062 autopsy reports of fetuses initially reviewed, 418 were included in the study for developing standard curves and tables. These included autopsies performed in the context of abortion ($n = 169$, 40.4%), medical termination of pregnancy ($n = 179$, 42.8%), intrauterine death/stillbirth ($n = 51$, 12.2%), and early neonatal death ($n = 19$, 4.5%). The clinically estimated age ranged from 12 to 42 gestational weeks. There were 196 (47.9%) females and 213 (52.1%) males. Gender data was either missing or ambiguous in 9 fetuses. The total number of cases for each gestational age showed great variation, with a mean of 13 and median of 7 (range 1, 45) cases per gestational age week (supplementary table—Online Resource 2). Of notice, fetuses with < 24 weeks of gestational age constituted the vast majority of our sample, with a mean of 27 (range 17, 45) cases per week. For gestational age ≥ 24 weeks, the number of cases did not exceed 10 for each week, with a mean of 5 cases per week. Similarly, for each parameter, there was a great variation of sample size, mainly due to the partial exclusion criteria and missing values. The median number of cases per parameter was 364 [range 99 (IND), 393 (FL)] for biometrical parameters; 325.5 [range 307 (brain weight), 367 (liver weight)] for organ weights; and 304 [range 294 (fibula length), 366 (femur length)]) for long bone lengths.

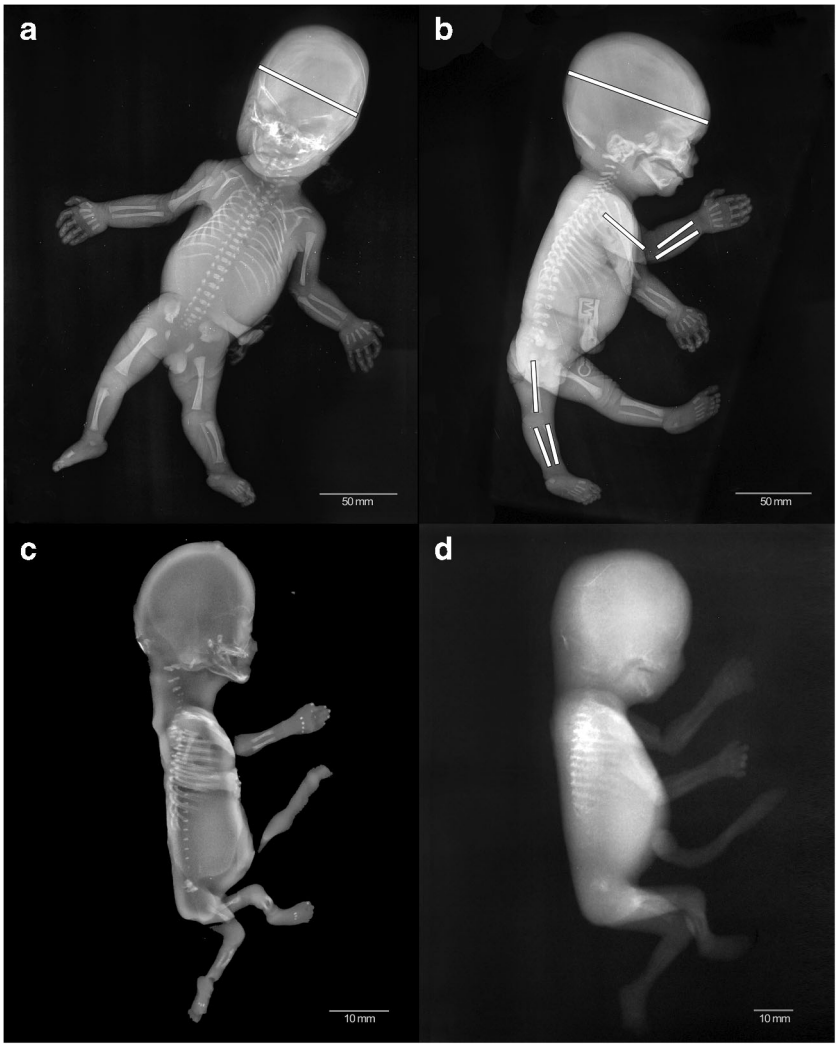


**Fig. 2** Examples of fetal biometric and long bone lengths taken using radiographs obtained before autopsy examination, using a standardized method. The body and the limbs are fixed to the examination plate: for the antero-posterior view, the upper extremities at the sides, slightly flexed at the elbows, with external rotation of the arms, supine position of the hands and the fingers extended; the lower limbs are positioned in abduction with the knees flat on the plate; for the lateral view, the left limbs are fixed to the table and the right limbs are positioned at different angles avoiding superposition of skeletal limb structures. **a**, **b** Conventional X-ray of a 22 gestational week fetus exemplifying the measurement of biparietal diameter, fronto-occipital diameter and long bone lengths. Biparietal diameter (**a**) is measured between the farthest points of parietal bones on the antero-posterior view coronal plane. Fronto-occipital diameter (**b**) is measured from the prominent point of the mid-frontal bone to the most prominent point of occipital bone on the lateral view. Long bone lengths (**b**) are measured on the lateral view on the limbs fixed to the examination plate by placing a line parallel to the long axis along the diaphysis (i.e., ossified shaft of the developing bone). **c** Whole body Faxitron of a 12-gestational-week fetus, highlighting the high image quality of this technique making it adequate for the evaluation of small fetuses, as opposed to **d** Conventional X-ray of a 14-gestational-week fetus with poor image quality

## Standard growth charts and tables

The expected means and SDs at various gestational ages, calculated and fitted based on our dataset, are presented in tables for each of biometric parameters (Table 1), organ weights (Table 2), and long bone lengths (Table 3). Charts of the fitted mean with 5th and 95th percentiles, superimposed on scatters of raw data, are shown for biometric parameters (Fig. 3), organ weights (Fig. 4), and long bone lengths (Fig. 5). Simpler charts for daily practice, showing curves of the fitted mean 3rd, 5th, 10th, 25th, 75th, 90th, 95th, and 97th centiles, are given in supplementary figures (Online Resource 3).

For most parameters, a quadratic or a cubic polynomial regression was chosen. Exceptions included inner and outer canthal distances, and philtrum length for which we best fitted a logarithmic model; internipple distance, fitted with a linear model and liver weight, fitted with a quartic polynomial model. Detailed mathematical equations and corresponding $R^2$ values are presented in a supplementary table (Online Resource 4). As expected, all

**Table 1** Fetal autopsy standards for biometric measurements (mean ± SD) at 12 to 42 weeks of gestation

| Gestational age (weeks) | BW (g) | CHL (mm) | CRL (mm) | HC (mm) | BPD (mm) | FOD (mm) | CC (mm) | AC (mm) | HL (mm) | FL (mm) | ICD (mm) | OCD (mm) | PL (mm) | IND (mm) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 12 | 21.1 ± 5.6 | 84.9 ± 18.6 | 61.0 ± 11.9 | 64.5 ± 11.2 | 17.6 ± 3.7 | 21.6 ± 2.5 | 55.7 ± 9.1 | 52.4 ± 10.7 | 8.2 ± 2.1 | 8.5 ± 2.5 | 5.4 ± 1.3 | 11.5 ± 2.4 | 1.5 ± 0.6 | 11.5 ± 1.9 |
| 13 | 25.2 ± 11.5 | 107.4 ± 18.9 | 76.1 ± 12.2 | 79.6 ± 11.5 | 21.6 ± 3.8 | 26.6 ± 2.7 | 68.2 ± 9.7 | 64.6 ± 11.4 | 10.9 ± 2.2 | 11.8 ± 2.5 | 6.6 ± 1.3 | 15.1 ± 2.5 | 2.0 ± 0.6 | 13.8 ± 2.1 |
| 14 | 39.1 ± 18.2 | 129.3 ± 19.2 | 90.9 ± 12.5 | 94.2 ± 11.9 | 25.6 ± 3.8 | 31.5 ± 3.0 | 80.4 ± 10.4 | 76.5 ± 12.1 | 13.5 ± 2.2 | 15.1 ± 2.6 | 7.6 ± 1.4 | 18.4 ± 2.5 | 2.5 ± 0.6 | 16.1 ± 2.2 |
| 15 | 62.5 ± 25.8 | 150.7 ± 19.5 | 105.4 ± 12.7 | 108.4 ± 12.2 | 29.4 ± 3.9 | 36.3 ± 3.2 | 92.4 ± 11.0 | 88.3 ± 12.8 | 16.2 ± 2.3 | 18.3 ± 2.7 | 8.6 ± 1.4 | 21.6 ± 2.6 | 2.9 ± 0.6 | 18.3 ± 2.4 |
| 16 | 95.2 ± 34.2 | 171.6 ± 19.8 | 119.5 ± 13.0 | 122.3 ± 12.5 | 33.2 ± 3.9 | 40.9 ± 3.5 | 104.2 ± 11.6 | 99.9 ± 13.6 | 18.8 ± 2.4 | 21.5 ± 2.8 | 9.5 ± 1.4 | 24.5 ± 2.6 | 3.3 ± 0.7 | 20.6 ± 2.6 |
| 17 | 137.0 ± 43.5 | 192.0 ± 20.0 | 133.3 ± 13.2 | 135.7 ± 12.8 | 36.8 ± 4.0 | 45.5 ± 3.7 | 115.7 ± 12.3 | 111.4 ± 14.3 | 21.3 ± 2.5 | 24.6 ± 2.9 | 10.4 ± 1.4 | 27.2 ± 2.7 | 3.6 ± 0.7 | 22.9 ± 2.7 |
| 18 | 187.8 ± 53.7 | 211.9 ± 20.3 | 146.7 ± 13.5 | 148.8 ± 13.1 | 40.4 ± 4.0 | 49.9 ± 3.9 | 127.0 ± 12.9 | 122.6 ± 15.0 | 23.9 ± 2.5 | 27.7 ± 3.0 | 11.2 ± 1.5 | 29.8 ± 2.7 | 4.0 ± 0.7 | 25.2 ± 2.9 |
| 19 | 247.5 ± 64.8 | 231.2 ± 20.6 | 159.8 ± 13.7 | 161.4 ± 13.4 | 43.9 ± 4.1 | 54.2 ± 4.2 | 138.0 ± 13.5 | 133.7 ± 15.7 | 26.3 ± 2.6 | 30.7 ± 3.1 | 11.9 ± 1.5 | 32.2 ± 2.8 | 4.3 ± 0.7 | 27.4 ± 3.1 |
| 20 | 315.7 ± 76.7 | 250.1 ± 20.9 | 172.6 ± 14.0 | 173.7 ± 13.7 | 47.3 ± 4.1 | 58.4 ± 4.4 | 148.8 ± 14.2 | 144.6 ± 16.4 | 28.8 ± 2.7 | 33.7 ± 3.1 | 12.6 ± 1.5 | 34.5 ± 2.8 | 4.6 ± 0.7 | 29.7 ± 3.2 |
| 21 | 392.3 ± 89.5 | 268.4 ± 21.2 | 185.1 ± 14.2 | 185.6 ± 14.0 | 50.7 ± 4.2 | 62.5 ± 4.6 | 159.4 ± 14.8 | 155.4 ± 17.1 | 31.2 ± 2.8 | 36.6 ± 3.2 | 13.3 ± 1.5 | 36.7 ± 2.9 | 4.9 ± 0.8 | 32.0 ± 3.4 |
| 22 | 477.1 ± 103.1 | 286.2 ± 21.5 | 197.2 ± 14.5 | 197.0 ± 14.4 | 53.9 ± 4.2 | 66.5 ± 4.9 | 169.7 ± 15.5 | 166.0 ± 17.8 | 33.6 ± 2.8 | 39.5 ± 3.3 | 14.0 ± 1.6 | 38.8 ± 2.9 | 5.2 ± 0.8 | 34.3 ± 3.6 |
| 23 | 570.0 ± 117.6 | 303.5 ± 21.7 | 209.0 ± 14.7 | 208.1 ± 14.7 | 57.1 ± 4.3 | 70.3 ± 5.1 | 179.8 ± 16.1 | 176.3 ± 18.5 | 35.9 ± 2.9 | 42.3 ± 3.4 | 14.6 ± 1.6 | 40.8 ± 3.0 | 5.5 ± 0.8 | 36.6 ± 3.7 |
| 24 | 670.8 ± 132.9 | 320.3 ± 22.0 | 220.4 ± 15.0 | 218.8 ± 15.0 | 60.1 ± 4.3 | 74.1 ± 5.4 | 189.7 ± 16.7 | 186.6 ± 19.2 | 38.2 ± 3.0 | 45.1 ± 3.5 | 15.2 ± 1.6 | 42.7 ± 3.0 | 5.7 ± 0.8 | 38.8 ± 3.9 |
| 25 | 779.2 ± 149.2 | 336.6 ± 22.3 | 231.6 ± 15.3 | 229.0 ± 15.3 | 63.1 ± 4.4 | 77.7 ± 5.6 | 199.3 ± 17.4 | 196.6 ± 19.9 | 40.5 ± 3.1 | 47.8 ± 3.6 | 15.8 ± 1.6 | 44.5 ± 3.1 | 6.0 ± 0.9 | 41.1 ± 4.1 |
| 26 | 895.1 ± 166.3 | 352.3 ± 22.6 | 242.3 ± 15.5 | 238.9 ± 15.6 | 66.0 ± 4.4 | 81.2 ± 5.8 | 208.7 ± 18.0 | 206.5 ± 20.6 | 42.8 ± 3.1 | 50.5 ± 3.6 | 16.3 ± 1.7 | 46.3 ± 3.1 | 6.2 ± 0.9 | 43.4 ± 4.2 |
| 27 | 1018.3 ± 184.2 | 367.5 ± 22.9 | 252.8 ± 15.8 | 248.4 ± 15.9 | 68.8 ± 4.5 | 84.6 ± 6.1 | 217.9 ± 18.7 | 216.2 ± 21.3 | 45.0 ± 3.2 | 53.1 ± 3.7 | 16.9 ± 1.7 | 48.0 ± 3.2 | 6.5 ± 0.9 | 45.7 ± 4.4 |
| 28 | 1148.7 ± 203.0 | 382.3 ± 23.1 | 262.9 ± 16.0 | 257.5 ± 16.2 | 71.6 ± 4.5 | 87.9 ± 6.3 | 226.8 ± 19.3 | 225.7 ± 22.0 | 47.1 ± 3.3 | 55.7 ± 3.8 | 17.4 ± 1.7 | 49.6 ± 3.2 | 6.7 ± 0.9 | 47.9 ± 4.6 |
| 29 | 1286.0 ± 222.7 | 396.5 ± 23.4 | 272.7 ± 16.3 | 266.2 ± 16.5 | 74.2 ± 4.6 | 91.1 ± 6.5 | 235.5 ± 19.9 | 235.1 ± 22.8 | 49.2 ± 3.4 | 58.2 ± 3.9 | 17.9 ± 1.7 | 51.2 ± 3.3 | 6.9 ± 1.0 | 50.2 ± 4.8 |
| 30 | 1430.0 ± 243.3 | 410.2 ± 23.7 | 282.2 ± 16.5 | 274.5 ± 16.8 | 76.8 ± 4.6 | 94.1 ± 6.8 | 244.0 ± 20.6 | 244.3 ± 23.5 | 51.3 ± 3.5 | 60.7 ± 4.0 | 18.4 ± 1.7 | 52.7 ± 3.3 | 7.1 ± 1.0 | 52.5 ± 4.9 |
| 31 | 1580.6 ± 264.7 | 423.3 ± 24.0 | 291.3 ± 16.8 | 282.4 ± 17.2 | 79.3 ± 4.7 | 97.1 ± 7.0 | 252.2 ± 21.2 | 253.3 ± 24.2 | 53.4 ± 3.5 | 63.1 ± 4.1 | 18.8 ± 1.8 | 54.2 ± 3.4 | 7.3 ± 1.0 | 54.8 ± 5.1 |
| 32 | 1737.6 ± 286.9 | 436.0 ± 24.3 | 300.1 ± 17.0 | 289.9 ± 17.5 | 81.6 ± 4.8 | 99.9 ± 7.3 | 260.2 ± 21.8 | 262.1 ± 24.9 | 55.4 ± 3.6 | 65.5 ± 4.2 | 19.3 ± 1.8 | 55.6 ± 3.4 | 7.5 ± 1.0 | 57.0 ± 5.3 |
| 33 | 1900.8 ± 310.1 | 448.1 ± 24.5 | 308.5 ± 17.3 | 297.0 ± 17.8 | 84.0 ± 4.8 | 102.6 ± 7.5 | 267.9 ± 22.5 | 270.7 ± 25.6 | 57.4 ± 3.7 | 67.8 ± 4.2 | 19.7 ± 1.8 | 57.0 ± 3.5 | 7.7 ± 1.0 | 59.3 ± 5.4 |
| 34 | 2070.1 ± 334.1 | 459.8 ± 24.8 | 316.6 ± 17.5 | 303.7 ± 18.1 | 86.2 ± 4.9 | 105.2 ± 7.7 | 275.4 ± 23.1 | 279.2 ± 26.3 | 59.3 ± 3.8 | 70.1 ± 4.3 | 20.1 ± 1.8 | 58.4 ± 3.5 | 7.9 ± 1.1 | 61.6 ± 5.6 |
| 35 | 2245.1 ± 358.9 | 470.9 ± 25.1 | 324.4 ± 17.8 | 310.0 ± 18.4 | 88.3 ± 4.9 | 107.7 ± 8.0 | 282.7 ± 23.8 | 287.5 ± 27.0 | 61.3 ± 3.8 | 72.3 ± 4.4 | 20.5 ± 1.9 | 59.7 ± 3.6 | 8.0 ± 1.1 | 63.9 ± 5.8 |
| 36 | 2425.8 ± 384.6 | 481.5 ± 25.4 | 331.9 ± 18.1 | 316.0 ± 18.7 | 90.4 ± 5.0 | 110.0 ± 8.2 | 289.7 ± 24.4 | 295.7 ± 27.7 | 63.1 ± 3.9 | 74.5 ± 4.5 | 20.9 ± 1.9 | 60.9 ± 3.6 | 8.2 ± 1.1 | 66.1 ± 5.9 |
| 37 | 2612.0 ± 411.2 | 491.6 ± 25.7 | 339.0 ± 18.3 | 321.5 ± 19.0 | 92.3 ± 5.0 | 112.3 ± 8.4 | 296.5 ± 25.0 | 303.6 ± 28.4 | 65.0 ± 4.0 | 76.6 ± 4.6 | 21.3 ± 1.9 | 62.2 ± 3.7 | 8.4 ± 1.1 | 68.4 ± 6.1 |
| 38 | 2803.5 ± 438.7 | 501.1 ± 25.9 | 345.8 ± 18.6 | 326.6 ± 19.3 | 94.2 ± 5.1 | 114.4 ± 8.7 | 303.1 ± 25.7 | 311.4 ± 29.1 | 66.8 ± 4.1 | 78.6 ± 4.7 | 21.7 ± 1.9 | 63.4 ± 3.7 | 8.5 ± 1.2 | 70.7 ± 6.3 |
| 39 | 3000.0 ± 467.0 | 510.2 ± 26.2 | 352.2 ± 18.8 | 331.4 ± 19.6 | 96.0 ± 5.1 | 116.5 ± 8.9 | 309.4 ± 26.3 | 319.0 ± 29.8 | 68.5 ± 4.1 | 80.7 ± 4.7 | 22.0 ± 2.0 | 64.5 ± 3.8 | 8.7 ± 1.2 | 73.0 ± 6.4 |
| 40 | 3201.5 ± 496.2 | 518.7 ± 26.5 | 358.4 ± 19.1 | 335.7 ± 20.0 | 97.7 ± 5.2 | 118.4 ± 9.2 | 315.5 ± 26.9 | 326.5 ± 30.5 | 70.3 ± 4.2 | 82.6 ± 4.8 | 22.4 ± 2.0 | 65.7 ± 3.8 | 8.9 ± 1.2 | 75.2 ± 6.6 |
| 41 | 3407.7 ± 526.2 | 526.8 ± 26.8 | 364.1 ± 19.3 | 339.6 ± 20.3 | 99.3 ± 5.2 | 120.2 ± 9.4 | 321.4 ± 27.6 | 333.7 ± 31.2 | 72.0 ± 4.3 | 84.6 ± 4.9 | 22.8 ± 2.0 | 66.8 ± 3.9 | 9.0 ± 1.2 | 77.5 ± 6.8 |
| 42 | 3618.4 ± 557.1 | 534.3 ± 27.1 | 369.6 ± 19.6 | 343.2 ± 20.6 | 100.9 ± 5.3 | 121.8 ± 9.6 | 327.0 ± 28.2 | 340.8 ± 31.9 | 73.6 ± 4.4 | 86.4 ± 5.0 | 23.1 ± 2.0 | 67.9 ± 3.9 | 9.1 ± 1.3 | 79.8 ± 6.9 |

Body weight (BW), crown-heel length (CHL), crown-rump length (CRL), head circumference (HC), biparietal diameter (BPD), fronto-occipital diameter (FOD), chest circumference (CC), abdominal circumference (AC), hand length (HL), foot length (FL), inner canthal distance (ICD), outer canthal distance (OCD), philtrum length (PL), and internipple distance (IND)

**Table 2** Fetal autopsy standards for organ weights (mean ± SD) at 12 to 42 weeks of gestation

| Gestational age (weeks) | Brain (g) | Heart (g) | Liver (g) | Lungs (g) | Kidneys (g) | Adrenals (g) | Spleen (g) | Thymus (g) |
|---|---|---|---|---|---|---|---|---|
| 12 | 5.17 ± 1.89 | 0.15 ± 0.01 | 1.24 ± 0.38 | 0.64 ± 0.01 | 0.27 ± 0.06 | 0.15 ± 0.07 | 0.01 ± 0.00 | 0.02 ± 0.01 |
| 13 | 5.80 ± 2.64 | 0.22 ± 0.01 | 1.28 ± 0.57 | 0.99 ± 0.36 | 0.27 ± 0.11 | 0.24 ± 0.12 | 0.02 ± 0.01 | 0.03 ± 0.01 |
| 14 | 7.84 ± 3.46 | 0.33 ± 0.10 | 1.94 ± 0.83 | 1.53 ± 0.72 | 0.33 ± 0.17 | 0.34 ± 0.16 | 0.02 ± 0.01 | 0.03 ± 0.01 |
| 15 | 11.24 ± 4.32 | 0.48 ± 0.17 | 3.16 ± 1.15 | 2.25 ± 1.09 | 0.51 ± 0.24 | 0.46 ± 0.20 | 0.03 ± 0.01 | 0.13 ± 0.05 |
| 16 | 15.97 ± 5.24 | 0.68 ± 0.24 | 4.87 ± 1.53 | 3.15 ± 1.47 | 0.80 ± 0.32 | 0.60 ± 0.25 | 0.04 ± 0.02 | 0.13 ± 0.05 |
| 17 | 21.98 ± 6.22 | 0.93 ± 0.32 | 7.04 ± 1.98 | 4.21 ± 1.86 | 1.20 ± 0.41 | 0.75 ± 0.30 | 0.07 ± 0.04 | 0.16 ± 0.07 |
| 18 | 29.24 ± 7.25 | 1.21 ± 0.41 | 9.61 ± 2.49 | 5.44 ± 2.26 | 1.70 ± 0.51 | 0.91 ± 0.36 | 0.13 ± 0.07 | 0.23 ± 0.10 |
| 19 | 37.69 ± 8.34 | 1.55 ± 0.50 | 12.53 ± 3.06 | 6.82 ± 2.67 | 2.30 ± 0.62 | 1.09 ± 0.42 | 0.23 ± 0.11 | 0.34 ± 0.15 |
| 20 | 47.31 ± 9.48 | 1.92 ± 0.60 | 15.77 ± 3.70 | 8.34 ± 3.09 | 2.99 ± 0.73 | 1.28 ± 0.47 | 0.36 ± 0.15 | 0.48 ± 0.21 |
| 21 | 58.05 ± 10.67 | 2.35 ± 0.71 | 19.30 ± 4.40 | 10.01 ± 3.52 | 3.76 ± 0.86 | 1.49 ± 0.54 | 0.53 ± 0.20 | 0.66 ± 0.28 |
| 22 | 69.87 ± 11.92 | 2.81 ± 0.82 | 23.08 ± 5.17 | 11.81 ± 3.96 | 4.62 ± 1.00 | 1.71 ± 0.60 | 0.73 ± 0.25 | 0.88 ± 0.38 |
| 23 | 82.74 ± 13.23 | 3.32 ± 0.94 | 27.10 ± 5.99 | 13.73 ± 4.41 | 5.56 ± 1.15 | 1.95 ± 0.67 | 0.97 ± 0.31 | 1.12 ± 0.48 |
| 24 | 96.60 ± 14.59 | 3.88 ± 1.06 | 31.35 ± 6.89 | 15.77 ± 4.87 | 6.57 ± 1.30 | 2.20 ± 0.74 | 1.24 ± 0.38 | 1.41 ± 0.61 |
| 25 | 111.42 ± 16.00 | 4.48 ± 1.19 | 35.79 ± 7.84 | 17.91 ± 5.34 | 7.65 ± 1.47 | 2.47 ± 0.81 | 1.55 ± 0.45 | 1.73 ± 0.74 |
| 26 | 127.16 ± 17.47 | 5.12 ± 1.33 | 40.44 ± 8.86 | 20.17 ± 5.82 | 8.79 ± 1.64 | 2.75 ± 0.89 | 1.89 ± 0.53 | 2.08 ± 0.90 |
| 27 | 143.78 ± 19.00 | 5.81 ± 1.47 | 45.29 ± 9.95 | 22.51 ± 6.31 | 9.99 ± 1.83 | 3.04 ± 0.97 | 2.26 ± 0.62 | 2.47 ± 1.06 |
| 28 | 161.23 ± 20.58 | 6.54 ± 1.62 | 50.35 ± 11.09 | 24.95 ± 6.81 | 11.25 ± 2.02 | 3.35 ± 1.05 | 2.67 ± 0.71 | 2.90 ± 1.25 |
| 29 | 179.48 ± 22.21 | 7.32 ± 1.77 | 55.61 ± 12.30 | 27.46 ± 7.32 | 12.56 ± 2.23 | 3.68 ± 1.13 | 3.12 ± 0.81 | 3.36 ± 1.44 |
| 30 | 198.49 ± 23.90 | 8.14 ± 1.93 | 61.10 ± 13.58 | 30.05 ± 7.84 | 13.91 ± 2.44 | 4.02 ± 1.22 | 3.60 ± 0.91 | 3.86 ± 1.66 |
| 31 | 218.22 ± 25.64 | 9.01 ± 2.10 | 66.84 ± 14.92 | 32.71 ± 8.37 | 15.30 ± 2.67 | 4.37 ± 1.31 | 4.11 ± 1.02 | 4.39 ± 1.89 |
| 32 | 238.62 ± 27.44 | 9.92 ± 2.27 | 72.84 ± 16.32 | 35.42 ± 8.91 | 16.73 ± 2.90 | 4.74 ± 1.40 | 4.66 ± 1.13 | 4.96 ± 2.13 |
| 33 | 259.66 ± 29.29 | 10.87 ± 2.45 | 79.14 ± 17.78 | 38.19 ± 9.45 | 18.19 ± 3.14 | 5.12 ± 1.49 | 5.24 ± 1.26 | 5.56 ± 2.39 |
| 34 | 281.29 ± 31.20 | 11.87 ± 2.64 | 85.78 ± 19.31 | 41.00 ± 10.01 | 19.67 ± 3.39 | 5.52 ± 1.59 | 5.86 ± 1.38 | 6.20 ± 2.66 |
| 35 | 303.47 ± 33.16 | 12.92 ± 2.83 | 92.79 ± 20.91 | 43.85 ± 10.58 | 21.18 ± 3.66 | 5.93 ± 1.69 | 6.51 ± 1.52 | 6.88 ± 2.95 |
| 36 | 326.17 ± 35.18 | 14.01 ± 3.03 | 100.22 ± 22.56 | 46.73 ± 11.16 | 22.70 ± 3.93 | 6.36 ± 1.79 | 7.20 ± 1.66 | 7.59 ± 3.25 |
| 37 | 349.34 ± 37.25 | 15.14 ± 3.23 | 108.12 ± 24.28 | 49.63 ± 11.75 | 24.24 ± 4.21 | 6.80 ± 1.90 | 7.93 ± 1.80 | 8.33 ± 3.57 |
| 38 | 372.95 ± 39.38 | 16.32 ± 3.44 | 116.54 ± 26.07 | 52.55 ± 12.35 | 25.78 ± 4.50 | 7.26 ± 2.01 | 8.68 ± 1.96 | 9.11 ± 3.91 |
| 39 | 396.94 ± 41.56 | 17.54 ± 3.66 | 125.55 ± 27.91 | 55.47 ± 12.95 | 27.33 ± 4.80 | 7.73 ± 2.12 | 9.47 ± 2.12 | 9.93 ± 4.26 |
| 40 | 421.29 ± 43.80 | 18.81 ± 3.88 | 135.20 ± 29.82 | 58.40 ± 13.57 | 28.87 ± 5.11 | 8.22 ± 2.23 | 10.30 ± 2.28 | 10.78 ± 4.62 |
| 41 | 445.95 ± 46.09 | 20.12 ± 4.11 | 145.58 ± 31.80 | 61.32 ± 14.20 | 30.41 ± 5.43 | 8.72 ± 2.35 | 11.16 ± 2.45 | 11.67 ± 5.00 |
| 42 | 470.88 ± 48.44 | 21.48 ± 4.35 | 156.76 ± 33.84 | 64.23 ± 14.84 | 31.93 ± 5.76 | 9.23 ± 2.47 | 12.06 ± 2.63 | 12.59 ± 5.40 |

anthropometric parameters were strongly correlated with gestational age. All $R^2$ values exceeded 0.90, except for inner canthal distance (0.85), philtrum length (0.83), thymus (0.76), spleen (0.89), and adrenals (0.85) weight. SD increased with gestational age, but anthropometric parameters showed different rates of increase. In general, biometric measurements and long bone lengths had narrower ranges of SD with less change with gestational age, while most organ weights showed marked increase of SD with gestational age.

## Discussion

Using standard references for autopsy anthropometric evaluation developed based on a sample of autopsied fetuses and neonates ensures that a fetus will be compared to others in the same circumstances. Yet, an autopsy sample per se implies a pathologic setting, raising questions about the "normality" of the reference population. In our study, several general and partial exclusion criteria were applied to minimize bias, allowing us to obtain a sample that we believe to be closely representative of autopsy normality. However, it is important to acknowledge that autopsy parameter standards should be regarded as "reference ranges" and not "normal ranges."

Our institution is a tertiary referral center that comprises a Prenatal Diagnostic Center, and thus approximately two-fifths of all autopsies performed refer to medical termination of pregnancies, followed by abortions representing approximately a third. By applying our meticulous criteria, we completely excluded more than half of our initial sample. Nevertheless,

**Table 3** Fetal autopsy standards for long bone lengths (mean ± SD) at 12 to 42 weeks of gestation

| Gestational age (weeks) | Humerus (mm) | Ulna (mm) | Radius (mm) | Femur (mm) | Tibia (mm) | Fibula (mm) |
|---|---|---|---|---|---|---|
| 12 | 6.3 ± 2.3 | 5.1 ± 1.8 | 5.0 ± 2.1 | 6.0 ± 2.5 | 4.7 ± 1.6 | 3.7 ± 1.4 |
| 13 | 9.7 ± 2.4 | 8.5 ± 1.9 | 8.0 ± 2.2 | 9.3 ± 2.5 | 7.7 ± 1.8 | 6.7 ± 1.6 |
| 14 | 13.0 ± 2.4 | 11.7 ± 2.1 | 10.8 ± 2.2 | 12.6 ± 2.6 | 10.7 ± 2.0 | 9.7 ± 1.9 |
| 15 | 16.2 ± 2.4 | 14.7 ± 2.2 | 13.5 ± 2.2 | 15.8 ± 2.6 | 13.6 ± 2.1 | 12.6 ± 2.2 |
| 16 | 19.2 ± 2.5 | 17.6 ± 2.4 | 16.1 ± 2.2 | 19.0 ± 2.7 | 16.5 ± 2.3 | 15.4 ± 2.5 |
| 17 | 22.1 ± 2.5 | 20.4 ± 2.5 | 18.5 ± 2.3 | 22.1 ± 2.7 | 19.2 ± 2.5 | 18.2 ± 2.7 |
| 18 | 24.9 ± 2.6 | 23.0 ± 2.8 | 20.9 ± 2.3 | 25.2 ± 2.8 | 21.9 ± 2.7 | 20.9 ± 3.0 |
| 19 | 27.6 ± 2.6 | 25.6 ± 2.8 | 23.0 ± 2.3 | 28.1 ± 2.8 | 24.6 ± 3.0 | 23.5 ± 3.0 |
| 20 | 30.1 ± 2.7 | 28.0 ± 2.8 | 25.1 ± 2.3 | 31.0 ± 2.9 | 27.2 ± 3.0 | 26.0 ± 3.0 |
| 21 | 32.6 ± 2.7 | 30.2 ± 2.8 | 27.1 ± 2.4 | 33.9 ± 3.0 | 29.7 ± 3.0 | 28.5 ± 3.0 |
| 22 | 35.0 ± 2.7 | 32.4 ± 2.8 | 29.0 ± 2.4 | 36.7 ± 3.0 | 32.2 ± 3.0 | 30.9 ± 3.0 |
| 23 | 37.3 ± 2.8 | 34.5 ± 2.8 | 30.7 ± 2.4 | 39.4 ± 3.1 | 34.6 ± 3.0 | 33.2 ± 3.0 |
| 24 | 39.5 ± 2.8 | 36.5 ± 2.8 | 32.4 ± 2.4 | 42.1 ± 3.1 | 36.9 ± 3.0 | 35.4 ± 3.0 |
| 25 | 41.6 ± 2.9 | 38.4 ± 2.8 | 34.0 ± 2.5 | 44.7 ± 3.2 | 39.2 ± 3.0 | 37.6 ± 3.0 |
| 26 | 43.6 ± 2.9 | 40.2 ± 2.8 | 35.6 ± 2.5 | 47.3 ± 3.2 | 41.4 ± 3.1 | 39.7 ± 3.0 |
| 27 | 45.5 ± 3.0 | 42.0 ± 2.7 | 37.1 ± 2.5 | 49.7 ± 3.3 | 43.5 ± 3.1 | 41.7 ± 3.0 |
| 28 | 47.4 ± 3.0 | 43.6 ± 2.7 | 38.5 ± 2.6 | 52.2 ± 3.3 | 45.6 ± 3.1 | 43.7 ± 3.0 |
| 29 | 49.2 ± 3.0 | 45.3 ± 2.7 | 39.8 ± 2.6 | 54.5 ± 3.4 | 47.6 ± 3.1 | 45.5 ± 3.0 |
| 30 | 51.0 ± 3.1 | 46.8 ± 2.7 | 41.1 ± 2.6 | 56.8 ± 3.4 | 49.6 ± 3.1 | 47.3 ± 3.0 |
| 31 | 52.6 ± 3.1 | 48.3 ± 2.7 | 42.4 ± 2.6 | 59.0 ± 3.5 | 51.5 ± 3.1 | 49.1 ± 3.0 |
| 32 | 54.3 ± 3.2 | 49.8 ± 2.7 | 43.6 ± 2.7 | 61.2 ± 3.6 | 53.3 ± 3.1 | 50.7 ± 3.0 |
| 33 | 55.8 ± 3.2 | 51.2 ± 2.7 | 44.9 ± 2.7 | 63.3 ± 3.6 | 55.1 ± 3.2 | 52.3 ± 3.0 |
| 34 | 57.4 ± 3.2 | 52.6 ± 2.7 | 46.0 ± 2.7 | 65.4 ± 3.7 | 56.8 ± 3.2 | 53.8 ± 3.0 |
| 35 | 58.8 ± 3.3 | 54.0 ± 2.7 | 47.2 ± 2.7 | 67.4 ± 3.7 | 58.4 ± 3.2 | 55.3 ± 3.0 |
| 36 | 60.3 ± 3.3 | 55.3 ± 2.7 | 48.4 ± 2.8 | 69.3 ± 3.8 | 60.0 ± 3.2 | 56.7 ± 3.0 |
| 37 | 61.7 ± 3.4 | 56.7 ± 2.6 | 49.6 ± 2.8 | 71.2 ± 3.8 | 61.5 ± 3.2 | 58.0 ± 3.0 |
| 38 | 63.1 ± 3.4 | 58.0 ± 2.6 | 50.7 ± 2.8 | 73.0 ± 3.9 | 63.0 ± 3.2 | 59.2 ± 3.0 |
| 39 | 64.4 ± 3.5 | 59.4 ± 2.6 | 51.9 ± 2.8 | 74.7 ± 3.9 | 64.4 ± 3.2 | 60.3 ± 3.1 |
| 40 | 65.7 ± 3.5 | 60.7 ± 2.6 | 53.1 ± 2.9 | 76.4 ± 4.0 | 65.7 ± 3.2 | 61.4 ± 3.1 |
| 41 | 67.0 ± 3.5 | 62.0 ± 2.6 | 54.3 ± 2.9 | 78.0 ± 4.0 | 66.9 ± 3.3 | 62.4 ± 3.1 |
| 42 | 68.3 ± 3.6 | 63.4 ± 2.6 | 55.6 ± 2.9 | 79.5 ± 4.1 | 68.1 ± 3.3 | 63.4 ± 3.1 |

the total number of cases included per each parameter is similar to studies previously performed in other countries.[7–9, 11, 13]

Our results emphasize the strong association between growth and gestational age, as well as a different increase in variability of the measurements with gestational age. Most biometric measurements and long bone lengths showed narrow ranges of variation. This contrasts with organ weights which showed greater variability, particularly in the third trimester. It is likely that organ weights are more sensible to changes induced by stress and illness than are other anthropometric parameters. Liver and spleen weight, for example, are highly dependent on fetal heart function and placental hemodynamic alterations. Lungs are frequently found altered in autopsies of neonates and stillbirths. Brain is an exception showing a narrow range of weight variation, in line with its known circulatory protective effect. Thymus stands out as the organ showing more weight variability, but it is not clear, if this can be considered a variation of normal or be related to immunologic changes.[19] Thymus and adrenals often show histological changes in association with intrauterine stress (frequently hypoxia) that can give a reasonable indication of the duration of fetal illness, which can explain at least part of the variation found in autopsy populations. Regarding long bone lengths, growth rates between 12 and 18th gestational week are similar for all six bones, and differences do not exceed 4 mm. Within this period, the humerus has approximately the same length or is slightly longer compared to the femur. Thereafter, lower limbs bones are longer and grow faster than the upper limb bones, with differences between the lengths increasing until term.

Appropriate model analysis is critical for creating accurate and consistent autopsy parameters standards [20]. Large

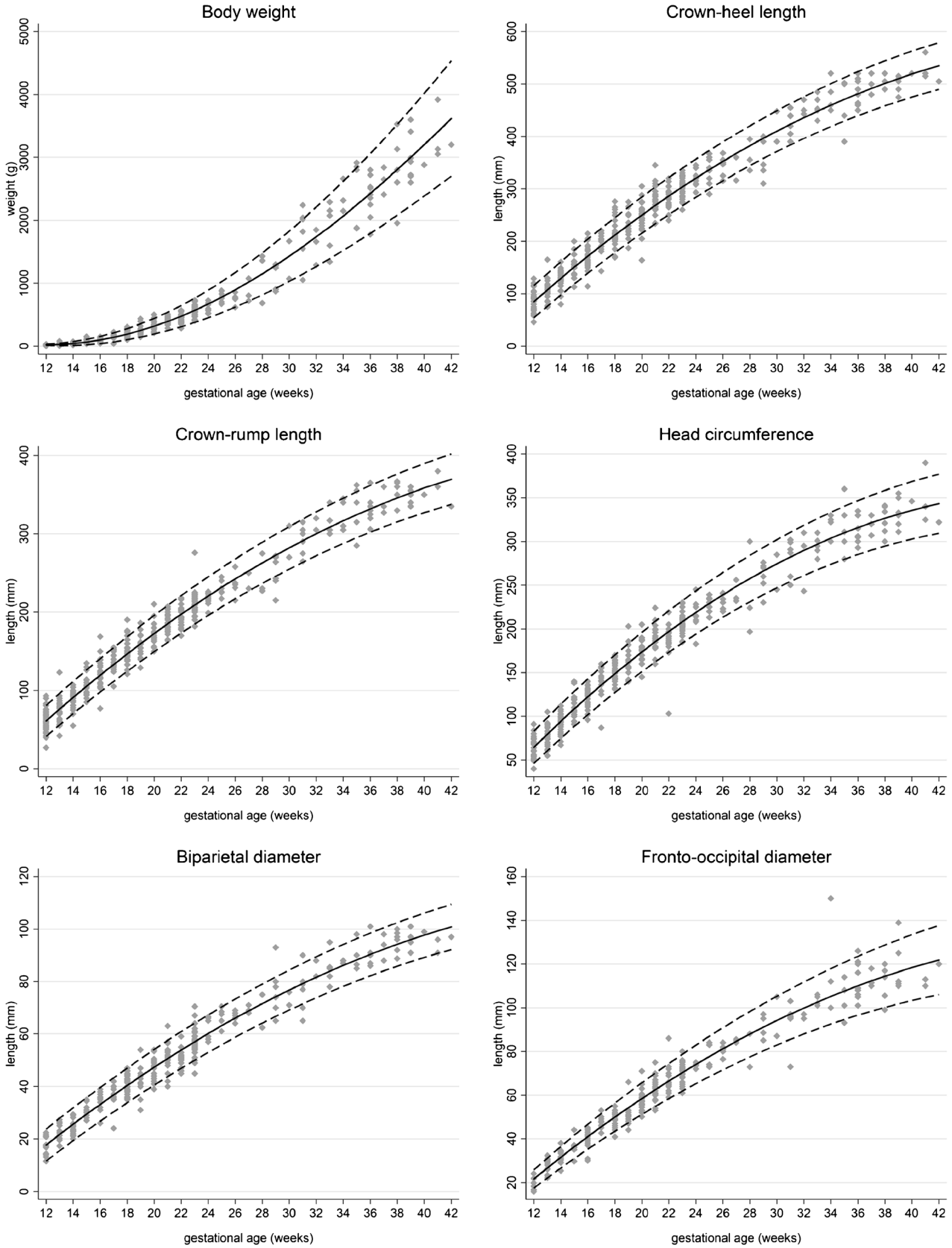


**Fig. 3** Plots of biometrical measurements showing scattered raw data and predicted mean, 5th and 95th centiles

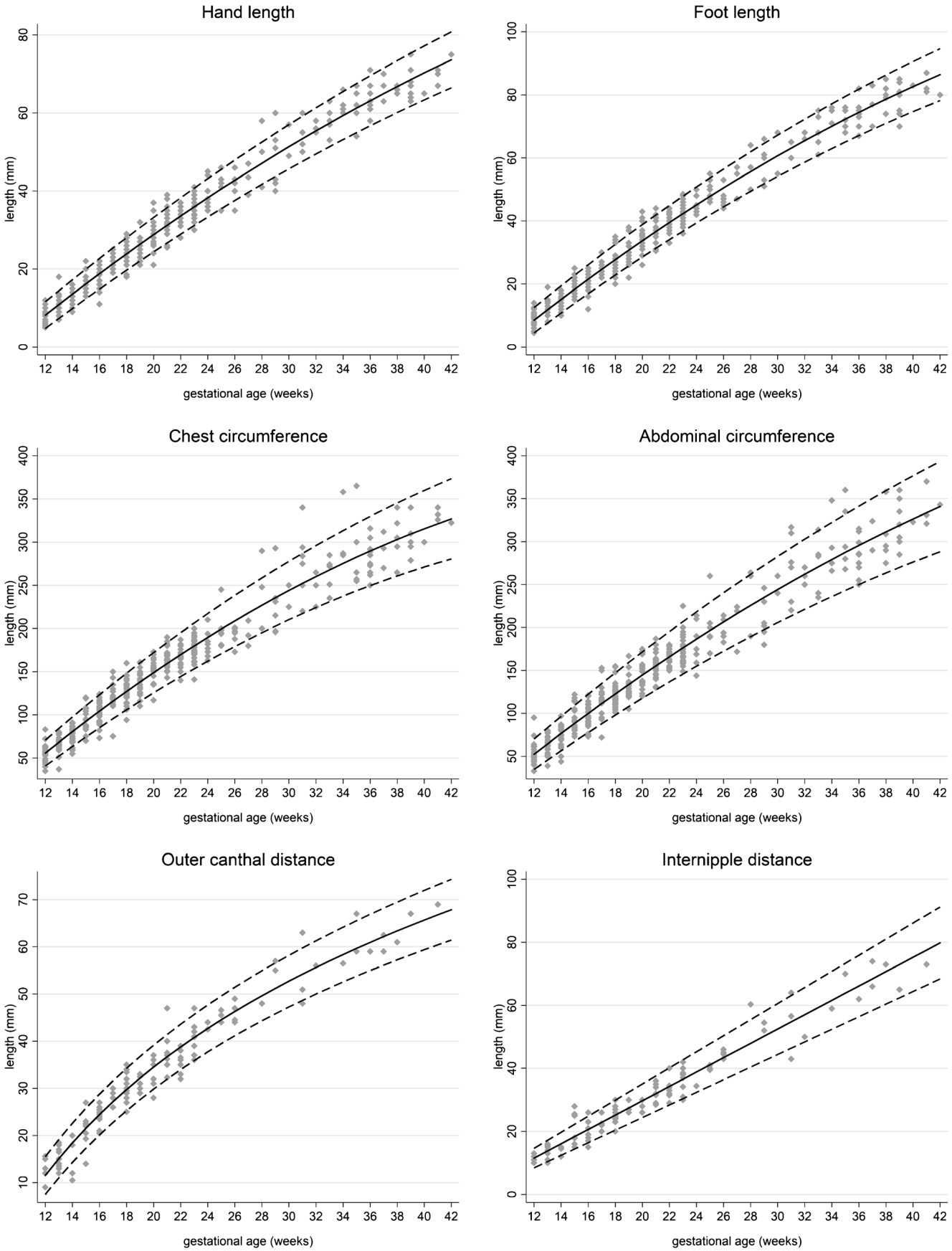


**Fig. 3** (continued)

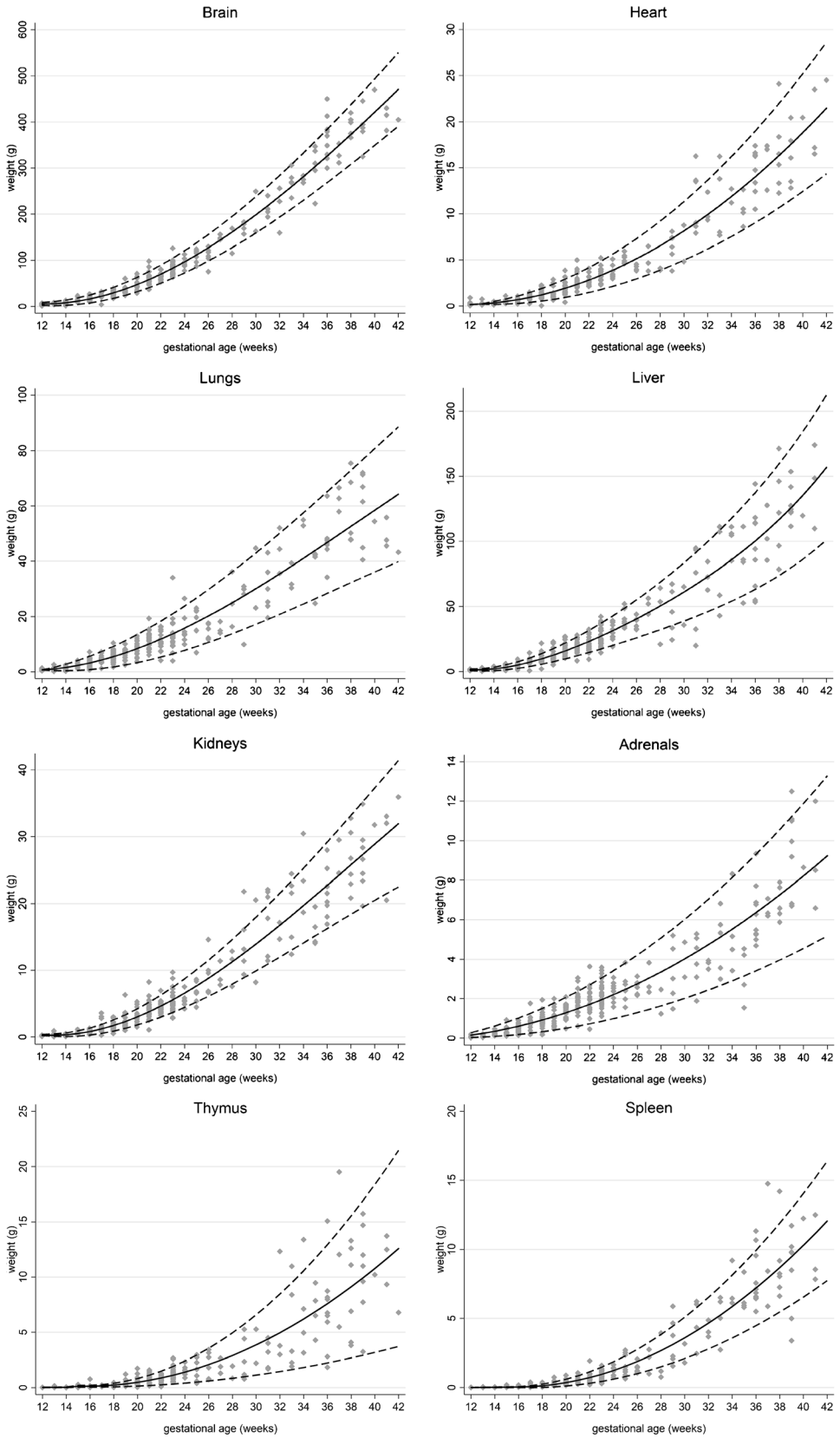


**Fig. 4** Plots of organ weights showing scattered raw data and predicted mean, 5th and 95th centiles

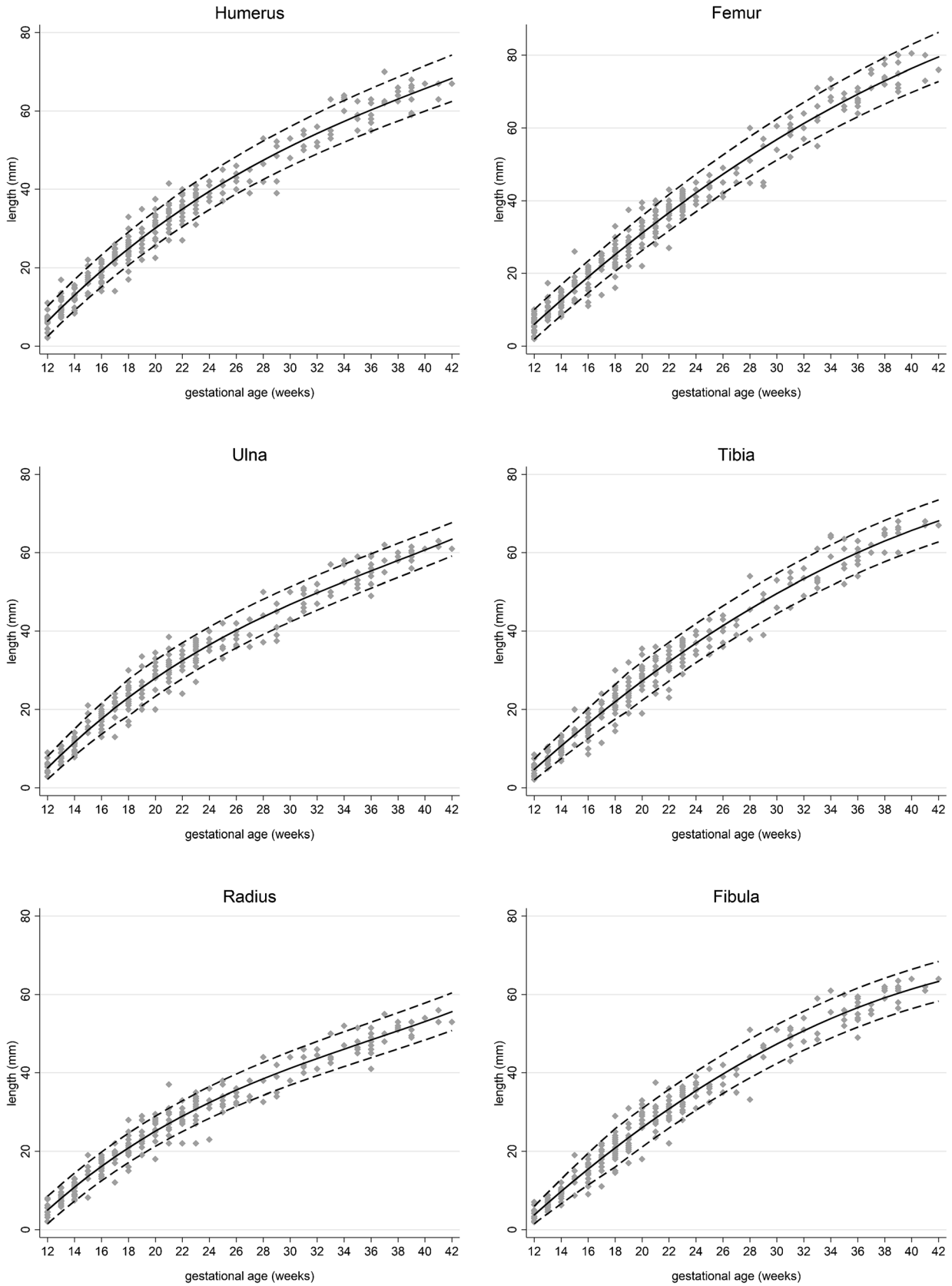


**Fig. 5** Plots of long bone lengths showing scattered raw data and predicted mean, 5th and 95th centiles

discrepancies are found between studies. As illustrated by Archie et al.[10] "consider a 26-week fetus whose brain weighs 130 g (…) depending on the standard used, the estimate varies: 56th, 69th, 98th, 95th, 81st, and 88th percentile. Thus, a pathologist might conclude that the brain weight was abnormally high or well within the normal range." By following Altman and Chitty's method, we were able to construct growth curves that change smoothly and take into account the change in variability across gestational age. We tested several mathematical models for each anthropometric parameter mean and SD. We believe that this thorough analysis, together with the rigorous sample selection, makes our standards reliable. In accordance with other authors, we found that quadratic or cubic polynomial models were the best fit for most biometric measurements and organ weight means.[7, 8, 11, 13] Regarding long bone lengths, some studies fitted linear models,[21–23] while others fitted, in our opinion, more suitable, non-linear models including logarithmic or polynomial models.[24, 25] Linear growth is not frequent for biological growth models, especially at the outer limits, and involves a systematic estimation bias in early and later gestational ages when compared to non-linear models. Indeed, in our study, the only parameter that was best fitted with a linear model was internipple distance, but the paucity of sample data for this parameter limits interpretation.[10]

It is important to develop standards representative of the target population, given the differences found between different population standards.[9, 11, 13, 26] Customized charts, such as standards for birthweight, have increasingly been implemented for clinical use.[26] For fetal autopsy parameters, examples of studies developing local standards include those originating from such different populations as USA,[1, 9] Denmark,[13] France,[7, 8] United Kingdom,[12] and Australia.[5, 6, 11] For the best of our knowledge, only one study, by Carneiro et al., aimed to develop standards for fetal autopsy parameters in the Portuguese population, focusing only on long bone lengths and using linear regression modeling.[22] Barata et al. did not establish standards but developed multiple regression models to predict gestational age, incorporating several anthropometric autopsy parameters.[27] Additionally, a few Portuguese studies establish standards based on live neonates and ultrasound measurements. Corte-Real et al. studied the growth pattern of the philtrum based on ultrasound measurements.[28] Sousa-Santos et al. describe a Portuguese birth weight standard from 23 to 42 weeks, with data from over 60,000 live-born neonates.[29] Even though ultrasound and live neonate standards can be of some use for autopsy examination, it is important to notice these measurements may differ from those in the autopsy setting.[10]

Specific variations in autopsy methodology may affect results of biometric measurements, organ weights, and long bone lengths, further supporting the importance of developing local standards. Organ weight may change depending on whether they are weighed fresh or after formalin fixation.[7] The most striking example is the brain. According to some authors, the brain gains weight with fixation, reaching up to 15% to 20% of the initial weight.[7, 30, 31] In our experience, we estimate a weight loss of fixated brains in the second trimester, of about 15%, probably related to the effect of NaCl in our fixative. Brain weight changes are dependent on gestational age, correlating to water content in brain tissue, and thus brain should be weighed fresh. Similar, but less striking, weight changes may occur in other organs. In Portugal, most autopsies of fetuses in the setting of medical termination of pregnancies and abortions are performed after a few hours of fixation, whereas stillbirths and neonatal deaths are performed fresh.

Linear biometric measurements are usually straightforward, whereas circumferential measurements may be prone to variation. Abdominal circumference is usually measured at the level of the umbilicus. However, this correlates poorly with ultrasound abdominal circumference measurement, probably the most important parameter for fetal growth restriction evaluation and birth weight estimation. Ultrasound landmarks for abdominal circumference are located in the upper abdomen including the umbilical vein branching to the right portal vein and visible stomach.[32] Thus, in our institution, autopsy abdominal circumference is measured near the border of the hepatic dullness. Radiographic measurements may also be prone to variation inherent to X-ray resolution. In our institution, when available, Faxitron equipment is used for fetuses with up to 17–20 weeks of gestational age and also, to obtain images with high resolution from digits, nasal bone, and in cases of skeletal dysplasia. Long bone measurements in conventional X-ray, particularly for radius and fibula, are less accurate for small fetuses (Fig. 2). Lastly, biparietal and fronto-occipital diameters in our practice are measured in X-ray, while the corresponding existent autopsy standards are based on caliper fetal head measurements.[6, 8]

Currently, the most frequently used growth charts and tables in Portuguese pathology labs for autopsy examination are those developed by Archie et al.[10] Indeed these standards are the most universal, given that they gather data from autopsies in different geographical populations as well as very different settings such as live term births, intrauterine fetal death/stillborn, and medical termination of pregnancy. In our study, by developing standards of a complete set of antropometric fetal parameters customized for our population, we ultimately hope to improve autopsy examination in the Portuguese population.

**Contributions** Liliana Costa and Nuno Botelho collected the data and pictures; Isabel Vilar and Marta Rodrigues constructed the database; Carla Bartosch designed the project, analyzed the data, and wrote the manuscript draft; Otilia Brandão supervised all the work and critically revised the manuscript text.

## Compliance with ethical standards

This study was conducted at the Centro Hospitalar S. João in Porto, Portugal, after being approved by the hospital's ethics committee (CES 334.15).

**Conflict of interest** The authors declare that they have no conflict of interest.

## References


1. Gruenwald P, Hoang Ngoc M (1960) Evaluation of body and organ weights in perinatal pathology. I. Normal standards derived from autopsies. Am J Clin Pathol 34:247–253
2. Schulz DM, Giordano DA, Schulz DH (1962) Weights of organs of fetuses and infants. Arch Pathol 74:244–250
3. Tanimura T, Nelson T, Hollingsworth RR, Shepard TH (1971) Weight standards for organs from early human fetuses. Anat Rec 171(2):227–236
4. McBride ML, Baillie J, Poland BJ (1984) Growth parameters in normal fetuses. Teratology. 29(2):185–191
5. Cussen L, Scurry J, Mitropoulos G, McTigue C, Gross J (1990) Mean organ weights of an Australian population of fetuses and infants. J Paediatr Child Health 26(2):101–103
6. Chambers HM, Knowles S, Staples A, Tamblyn M, Haan EA (1993) Anthropometric measurements in the second trimester fetus. Early Hum Dev 33(1):45–59
7. Guihard-Costa AM, Menez F, Delezoide AL (2002) Organ weights in human fetuses after formalin fixation: standards by gestational age and body weight. Pediatr Dev Pathol 5(6):559–578
8. Guihard-Costa AM, Menez F, Delezoide AL (2003) Standards for dysmorphological diagnosis in human fetuses. Pediatr Dev Pathol 6(5):427–434
9. Hansen K, Sung CJ, Huang C, Pinar H, Singer DB, Oyer CE (2003) Reference values for second trimester fetal and neonatal organ weights and measurements. Pediatr Dev Pathol 6(2):160–167
10. Archie JG, Collins JS, Lebel RR (2006) Quantitative standards for fetal and neonatal autopsy. Am J Clin Pathol 126(2):256–265
11. Phillips JB, Billson VR, Forbes AB (2009) Autopsy standards for fetal lengths and organ weights of an Australian perinatal population. Pathology. 41(6):515–526
12. Pryce JWBA, Ashworth MT, Kiho L, Malone M, Sebire NJ (2014) Reference ranges for organ weights of infants at autopsy: results of >1000 consecutive cases from a single centre. BMC Clin Pathol 14: 18
13. Maroun LL, Graem N (2005) Autopsy standards of body parameters and fresh organ weights in nonmacerated and macerated human fetuses. Pediatr Dev Pathol 8(2):204–217
14. Langley F (1971) The perinatal postmortem examination. J Clin Pathol 24(2):159–169
15. Valdés-Dapena MA, Huff DS (1983) Perinatal autopsy manual. The Institute
16. Laurini RN (1986) Aspects of developmental pathology. PhD thesis, Van Denderen
17. Altman DG (1993) Construction of age-related reference centiles using absolute residuals. Stat Med 12(10):917–924
18. Altman DG, Chitty LS (1994) Charts of fetal size: 1. Methodology. Br J Obstet Gynaecol 101(1):29–34
19. Kornstein M (1988) Immunopathology of the thymus: a review. Surg Pathol 1:248–272
20. Silverwood RJ, Cole TJ (2007) Statistical methods for constructing gestational age-related reference intervals and centile charts for fetal size. Ultrasound Obstet Gynecol 29(1):6–13
21. Elejalde BR, De Elejalde MM, Opitz JM, Reynolds JF, Hall JG (1986) The prenatal growth of the human body determined by the measurement of bones and organs by ultrasonography. Am J Med Genet 24(4):575–598
22. Carneiro C, Curate F, Cunha E (2016) A method for estimating gestational age of fetal remains based on long bone lengths. Int J Legal Med 130(5):1333–1341
23. Kasraeian M, Shahraki HR, Asadi N, Vafaei H, Sameni S (2017) Cross-sectional study of fetal long-bone length in an Iranian population at 17–25 weeks of gestation. Int J Gynecol Obstet 137(1):20–25
24. Chitty LS, Altman DG (2002) Charts of fetal size: limb bones. BJOG. 109(8):919–929
25. Brons J, Van Geijn H, Bezemer P, Nauta J, Arts NT (1990) The fetal skeleton; ultrasonographic evaluation of the normal growth. Eur J Obstet Gynecol Reprod Biol 34(1):21–36
26. Francis A, Hugh O, Gardosi J (2018) Customized vs INTERGROWTH-21(st) standards for the assessment of birthweight and stillbirth risk at term. Am J Obstet Gynecol 218(2S):S692–S699
27. Barata A, Carvalho L, Couto FM (2017) Anthropometric data analytics: a portuguese case study. In: Paper presented at: international conference on practical applications of computational biology & Bioinformatics2017
28. Côrte-Real I, Braga AC, Nogueira R, Felino A, Valente F, Vaz P (2016) Growth pattern of the philtrum in cases of normal and pathological fetal development. Rev Port Estomatol Med Dent Cir Maxilofac 57(4):223–228
29. Sousa-Santos RF, Miguelote RF, Cruz-Correia RJ, Santos CC, Bernardes JF (2016) Development of a birthweight standard and comparison with currently used standards. What is a 10th centile? Eur J Obstet Gynecol Reprod Biol 206:184–193
30. Larroche JC (1977) Developmental pathology of the neonate. Excerpta Medica
31. Quester R, Schröder R (1997) The shrinkage of the human brain stem during formalin fixation and embedding in paraffin. J Neurosci Methods 75(1):81–89
32. American Institute of Ultrasound in M (2013) AIUM practice guideline for the performance of obstetric ultrasound examinations. J Ultrasound Med 32(6):1083–1101
33. Boyd R (1861) Tables of the weights of the human body and internal organs in the sane and insane of both sexes at various ages, arranged from 2614 post-mortem examinations. Phil Trans Royal Soc London 151(Part I)
34. Kurmanavicius J, Wright EM, Royston P, Wisser J, Huch R, Huch A, Zimmermann R (1999) Fetal ultrasound biometry: 1. Head reference values. BJOG Int J Obstet Gynaecol 106(2):126–135
35. Kurmanavicius J, Wright EM, Royston P, Zimmermann R, Huch R, Huch A, Wisser J (1999) Fetal ultrasound biometry: 2. Abdomen and femur length reference values. BJOG Int J Obstet Gynaecol 106(2):136–143