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New patterns of the growing L3 vertebra and its 3 ossification centers in human fetuses – a CT, digital, and statistical study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ACDEF 1 **Michał Szpinda**
ABCDF 1 **Mariusz Baumgart**
CD 1 **Anna Szpinda**
CD 2 **Alina Woźniak**
CF 2 **Celestyna Mila-Kierzenkowska**

1 Department of Normal Anatomy, The Ludwik Rydygier Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland
2 Department of Medical Biology, The Ludwik Rydygier Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland

Corresponding Author: Michał Szpinda, e-mail: kizanat@cm.umk.pl
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Background: This study describes reference data for L3 vertebra and its 3 ossification centers at varying gestational ages.





Material/Methods: Using CT, digital-image analysis and statistics, the growth of L3 vertebra and its 3 ossification centers in 55 spontaneously aborted human fetuses aged 17–30 weeks was examined.

Results: Neither sex nor right-left significant differences were found. The height and transverse and sagittal diameters of the L3 vertebral body increased logarithmically. Its cross-sectional area followed linearly, whereas its volume increased parabolically. The transverse and sagittal diameters of the ossification center of the L3 vertebral body varied logarithmically, but its cross-sectional area and volume grew linearly. The ossification center-to-vertebral body volume ratio gradually declined with age. The neural ossification centers increased logarithmically in length and width, and proportionately in cross-sectional area and volume.

Conclusions: With no sex differences, the growth dynamics of the L3 vertebral body follow logarithmically in height, sagittal and transverse diameters, linearly (in cross-sectional area), and parabolically (in volume). The growth dynamics of the 3 ossification centers of the L3 vertebra follow logarithmically in transverse and sagittal diameters, and linearly (in cross-sectional area and volume). The age-specific reference intervals of the L3 vertebra and its 3 ossification centers present the normative values of clinical importance in the diagnosis of congenital spinal defects.

Key words: **typical lumbar vertebra • ossification center • dimensions • CT examination • digital-image analysis • skeletal dysplasias • human fetuses**

Full-text PDF: <http://www.basic.medscimonit.com/download/index/idArt/883956>

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Background

The advancing resolution capabilities of ultrasound devices have led to an increase in prenatal diagnostic examinations [1–7]. Knowledge of the normative growth of the spine is of great clinical relevance in the early recognition of spinal abnormalities [8–11] and skeletal dysplasias [12].

The typical lumbar vertebra is by far the largest vertebra; the average thoracic, cervical, and sacral vertebrae are 3/4, 1/2, and 2/5, respectively, of its length [13]. During the 6th week of gestation within primitive vertebral bodies 2 lateral chondrification centers arise, which at 7–8 weeks fuse to form the primary ossification center, transiently separated by the notochord remnant [11,14,15]. Each vertebra is ossified from the 3 primary centers, 1 in the vertebral body, and 1 in each neural arch [13,16]. The ossification centers for the neural arches and vertebral bodies develop in an independent pattern [13]. In the vertebral bodies, ossification first starts at the thoracolumbar junction in fetuses with the crown-rump length of 40–52 mm, and from there proceeds in a cephalocaudal direction [16,17]. On the contrary, 2 ossification patterns of neural arches have been proposed: originating in the 3 spinal regions (thoracolumbar, cervical-thoracic, and superior cervical) [18–20]; or in the midthoracic spine [16].

Although morphometric values for lumbar vertebrae in human fetuses have been presented by some authors [13,21–25], the quantitative analysis of vertebral ossification centers has recently been reported with relation to the C4 vertebra [26] and the C1–S5 vertebral bodies [27]. Because of this, in relation to the typical L3 lumbar vertebra, our objectives were set to determine the following:

- age-specific reference intervals for dimensions (height, transverse and sagittal diameters, cross-sectional area, and volume) of its vertebral body;
- age-specific reference intervals for dimensions (transverse and sagittal diameters, cross-sectional area, and volume) of its 3 ossification centers;
- the best-fit growth curves for each morphometric parameter studied;
- the relative growth of the ossification center within the vertebral body (the ossification center-to-vertebral body volume ratio).

Material and Methods

The present study was carried out on 55 human fetuses (27 males, 28 females) aged 17–30 weeks of Caucasian racial origin (Table 1), derived from spontaneous abortions or stillbirths in the years 1989–2001 because of placental insufficiency. Gestational age was determined from measurements

of the crown-rump length [28]. Legal and ethical considerations were approved by the University Research Ethics Committee (KB 275/2011). All the included specimens were diagnosed as normal, since both internal and external gross malformations had been ruled out on macroscopic examination. The fetuses underwent a CT examination with the reconstructed slice width option of 0.4 mm and the number of 128 slices acquired simultaneously using Biograph mCT (Siemens). There were no cases of morphological evidence of a spinal anomaly. The scans obtained were recorded in DICOM formats (Figure 1A), which allow 3-dimensional reconstructions and the morphometric analysis of objects chosen. Next, DICOM formats were assessed using digital image analysis of Osirix 3.9 (Figure 1B), which semi-automatically estimated linear (sagittal and transverse diameters, height, length, and width), 2-dimensional (cross-sectional area), and 3-dimensional (volume) parameters of vertebral bodies and ossification centers (Figure 1C, 1D). The contour of each L3 vertebral body and its 3 ossification centers were outlined with a cursor and stored.

For each fetus the following 5 measurements of the L3 vertebral body were taken:

- 1–3. height, transverse, and sagittal diameters;
4. cross-sectional area;
5. volume;

and the following 12 measurements of the 3 ossifications centers:

- within the vertebral body (6–9):
- 6, 7. transverse and sagittal diameters;
- 8. cross-sectional area
- 9. volume; and
- within the right and left neural processes (10–17):
- 10, 11. right and left lengths;
- 12, 13. right and left widths;
- 14, 15. right and left cross-sectional areas;
- 16, 17. right and left volumes.

In order to minimize measurement and observer bias, all the measurements were performed by 1 researcher (M.B). Each measurement was repeated 3 times under the same conditions, and the mean of the 3 was finally used. The intra-observer variation was evaluated using the Wilcoxon signed-rank test. All the parameters studied were plotted against fetal age to establish their growth dynamics. The relative growth of the vertebral body and its ossification center was expressed as the sagittal: transverse diameter ratios and the ossification center: vertebral body volume ratio. As the first step in the statistical analysis, Student's t-test was used to examine the influence of sex on the values obtained. In order to examine sex differences, we tested possible differences between the following 5 age groups: 17–19, 20–22, 23–25, 26–28, and 29–30 weeks. Furthermore, we tested sex differences for the whole sample, without taking into consideration fetal ages. To test whether

Table 1. Distribution of the fetuses studied.

Gestational age (weeks)	Crown- rump length (mm)				Number	Sex	
	Mean	SD	Min	Max		Male	Female
17	115.00		115.00	115.00	1	0	1
18	133.33	5.77	130.00	140.00	3	1	2
19	149.50	3.82	143.00	154.00	8	3	5
20	161.00	2.71	159.00	165.00	4	2	2
21	174.75	2.87	171.00	178.00	4	3	1
22	185.00	1.41	183.00	186.00	4	1	3
23	197.60	2.61	195.00	202.00	5	2	3
24	208.67	3.81	204.00	213.00	9	5	4
25	214.00		214.00	214.00	1	0	1
26	229.00	5.66	225.00	233.00	2	1	1
27	239.17	3.75	235.00	241.00	6	6	0
28	249.50	0.71	249.00	250.00	2	0	2
29	253.00	0.00	253.00	253.00	2	0	2
30	263.25	1.26	262.00	265.00	4	3	1
Total					55	27	28

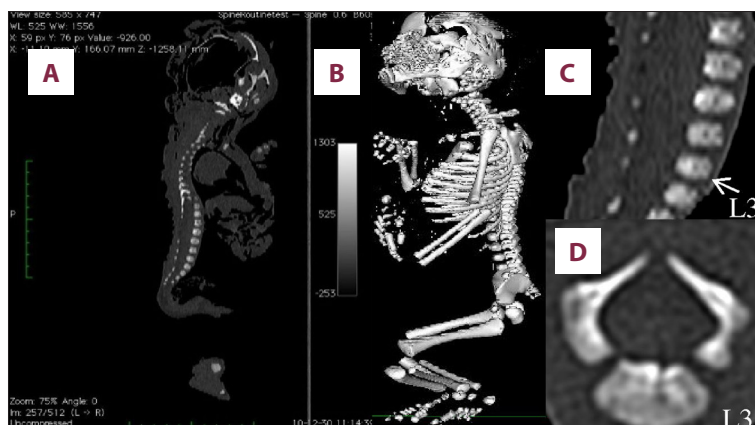


Figure 1. CT of a female fetus aged 24 weeks recorded in DICOM formats (A) and assessed by Osirix 3.9 (B) in the sagittal (C) and horizontal (D) planes.

the different variables significantly changed with age, the one-way ANOVA test and post-hoc RIR Tukey test were used for the 5 afore-mentioned groups. Linear and nonlinear regression analysis was used to derive the best-fit curve description for each parameter against gestational age as the independent parameter, with estimated coefficients of determination (R^2) between each parameter and fetal age.

Results

No significant differences were observed in the evaluation of intra-observer reproducibility of the vertebral measurements or in the values of the parameters studied according to sex. Thus, the values obtained for dimensions of the L3 vertebra

(Table 2) and its ossification centers (Tables 3 and 4) have been summarized for both sexes. By contrast, there was a highly significant correlation between each parameter and gestational age ($P=0.0000$). The numerical data correlated to age revealed differentiated growth dynamics, expressed by specific best-fit growth curves (Figures 2–7).

Dimensions of the L3 vertebral body are presented in Table 2. The values of the L3 vertebral body height increased from 3.86 to 6.08 ± 0.64 mm for fetuses at the age of 17 and 30 weeks, respectively. With regard to gestational age, the height of the L3 vertebral body (Figure 2A) showed an increase in accordance with the logarithmic function: $y = -11.335 + 5.061 \times \ln(\text{Age}) \pm 0.344$ ($R^2=0.84$). Between the ages of 17 and 30 weeks, the transverse diameter of the L3 vertebral body (Figure 2B) had

Table 2. Morphometric parameters of the L3 vertebral body.

Age (weeks)	n	Height (mm)		Transverse diameter (mm)		Sagittal diameter (mm)		Cross-sectional area (mm ²)		Volume (mm ³)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
17	1	3.86		3.14		2.94		8.10		23.17	
18	3	4.25	0.92	5.17	1.62	4.21	0.98	10.36	2.98	31.27	1.86
19	8	3.30	0.10	3.76	0.35	3.64	0.57	13.23	0.73	34.11	14.15
20	4	↓ (P<0.05) 3.57	0.42	↓ (P<0.01) 4.58	0.41	↓ (P<0.01) 4.15	0.45	↓ (P<0.01) 14.63	2.43	↓ (P<0.001) 53.21	11.03
21	4	4.46	0.41	5.99	0.53	3.74	0.05	18.58	0.93	83.05	12.16
22	4	4.35	0.34	6.08	0.66	4.29	0.29	21.80	1.07	95.26	12.68
23	5	↓ (P<0.05) 4.52	0.41	↓ (P<0.01) 6.35	0.43	↓ (P<0.01) 4.58	0.29	↓ (P<0.001) 23.94	2.17	↓ (P<0.001) 113.57	14.30
24	9	4.82	0.22	6.66	0.89	5.19	0.38	24.10	3.18	118.09	
25	1	4.90		6.55		5.20		27.19		129.26	1.01
26	2	↓ (P<0.01) 4.94	0.10	↓ (P<0.01) 7.53	0.04	↓ (P<0.01) 5.69	0.87	↓ (P<0.001) 39.20	0.99	↓ (P<0.001) 165.48	28.43
27	6	5.15	0.43	7.14	1.04	5.04	0.44	36.47	4.02	173.00	39.15
28	2	6.59	0.59	9.19	0.76	6.05	0.70	42.90	2.12	293.62	0.15
29	2	↓ (P<0.05) 5.25	0.01	↓ (P<0.05) 6.74	0.01	↓ (P<0.01) 6.55	0.01	↓ (P<0.05) 41.55	0.07	↓ (P<0.01) 283.60	31.02
30	4	6.08	0.64	8.34	0.54	6.20	0.14	43.10	1.44	262.47	32.04

values from 3.14 to 8.34±0.54 mm, following the logarithmic function: $y = -23.678 + 9.495 \times \ln(\text{Age}) \pm 0.674$ ($R^2 = 0.82$). During the analyzed period, the values of sagittal diameter of the L3 vertebral body (Figure 2C) were increasing logarithmically from 2.94 to 6.20±0.14 mm, according to the formula: $y = -13.510 + 5.816 \times \ln(\text{Age}) \pm 0.461$ ($R^2 = 0.79$). According to these logarithmic functions, at ages of 17 and 30 weeks the growth velocities (mm per week) for height and transverse and sagittal diameters of the L3 vertebral body were gradually declining with advanced fetal age ($P < 0.05$), from 0.29 to 0.17 mm, from 0.54 to 0.32 mm, and from 0.33 to 0.20 mm, respectively. The relative growth of the L3 vertebral body was not proportionate, because the transverse diameter grew much faster than the sagittal diameter, which was indicated by the decrease in the sagittal: transverse diameter ratio (Figure 2D) from 0.88±0.11 to 0.71±0.08 ($P = 0.0002$). The values of the cross-sectional area of the L3 vertebral body (Figure 3A) ranged from 8.10 to 43.10±1.44 mm² in fetuses aged 17 and 30 weeks, respectively, generating the linear function $y = -40.307 + 2.816 \times \text{Age} \pm 3.793$ ($R^2 = 0.88$). During the study period, the volumetric growth of the L3 vertebral body (Figure 3B), from 23.17 to 262.47±32.04 mm³, followed the quadratic regression $y = -105.233 + 0.417 \times \text{Age}^2 \pm 19.657$ ($R^2 = 0.93$).

Dimensions of ossification centers of the L3 vertebral body are presented in Table 3, which also presents the 3 ossification

centers of the L3 vertebral body (1), and right (2) and left (3) neural processes in fetuses aged 17, 22, 26, and 30 weeks. During the study period, the transverse (Figure 4A) and sagittal (Figure 4B) diameters of the ossification center of the L3 vertebral body increased logarithmically from 2.31 to 7.22±0.65 mm, and from 1.98 to 5.04±0.34 mm, according to the following models: $y = -27.610 + 10.341 \times \ln(\text{Age}) \pm 0.752$ ($R^2 = 0.82$) and $y = -13.858 + 5.636 \times \ln(\text{Age}) \pm 0.411$ ($R^2 = 0.82$), respectively. Thus, the growth dynamics for transverse and sagittal diameters declined with age, from 0.59 to 0.35 mm per week, and from 0.32 to 0.19 mm per week, respectively. During the study period, the sagittal: transverse diameter ratio of the ossification center (Figure 4C) decreased from 1.05±0.16 to 0.62±0.09. The cross-sectional area of ossification centers (Figure 4D) increased proportionately from 4.90 mm² in fetuses aged 17 weeks to 28.15±2.31 mm² in fetuses aged 30 weeks, according to the linear function: $y = -32.423 + 2.071 \times \text{Age} \pm 2.443$ ($R^2 = 0.91$). The volumetric growth of the ossification center (Figure 5A) from 14.50 to 41.65±3.36 mm³ followed proportionately as $y = -44.200 + 2.823 \times \text{Age} \pm 3.762$ ($R^2 = 0.88$).

The volumetric growth of the L3 vertebral body and its ossification center (Figure 5B) was presented in a relative manner using the ossification center: vertebral body volume ratio. As illustrated in Figure 5C, its value gradually declined from 0.24±0.06 to 0.14±0.05 during the study period.

Table 3. Morphometric parameters of the ossification center of L3 vertebra.

Age (weeks)	n	L3 vertebral body							
		Transverse diameter (mm)		Sagittal diameter (mm)		Cross-sectional area (mm ²)		Volume (mm ³)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
17	1	2.31		1.98		4.90		14.50	
18	3	3.94	1.96	3.27	0.77	7.73	1.16	13.06	1.98
19	8	2.16	0.53	2.45	0.35	4.39	0.78	5.79	1.05
20	4	↓ (P<0.01) 3.27	0.12	↓ (P<0.01) 3.26	0.33	↓ (P<0.01) 8.28	1.97	↓ (P<0.001) 12.58	2.52
21	4	4.92	0.51	3.40	0.08	12.83	1.42	17.25	1.91
22	4	4.80	0.70	3.54	0.44	13.83	1.55	18.45	1.07
23	5	↓ (P<0.01) 4.91	0.44	↓ (P<0.01) 3.47	0.87	↓ (P<0.01) 14.56	1.77	↓ (P<0.001) 19.50	2.68
24	9	5.26	0.87	4.17	0.39	16.41	2.31	22.26	3.88
25	1	5.37		3.87		15.90		23.10	
26	2	↓ (P<0.01) 6.08	0.47	↓ (P<0.01) 4.83	0.40	↓ (P<0.001) 24.05	0.21	↓ (P<0.001) 38.20	3.82
27	6	6.09	1.11	4.41	0.48	24.25	2.53	31.00	3.32
28	2	7.62	0.81	4.60	0.94	28.70	2.26	37.20	4.38
29	2	↓ (P<0.05) 5.84	0.01	↓ (P<0.05) 5.55	0.07	↓ (P<0.05) 24.15	0.07	↓ (P<0.05) 32.60	0.14
30	4	7.22	0.65	5.04	0.34	28.15	2.31	41.65	3.36

Dimensions of ossification centers of neural processes are given in Table 4. Although the right-left differences for the whole sample were not found to be statistically significant, the results for each neural process are presented separately because of their great inter-individual variability (Table 4). The length of the neural ossification centers ranged from 2.56 to 5.88±0.66 on the right (Figure 6A), and from 2.34 to 5.90±0.80 mm on the left (Figure 6B), according to the logarithmic functions: $y = -18.386 + 7.246 \times \ln(\text{Age}) \pm 0.585$ ($R^2 = 0.78$) and $y = -23.171 + 8.766 \times \ln(\text{Age}) \pm 0.753$ ($R^2 = 0.76$), respectively. Its width increased from 1.15 to 2.32±0.23 mm on the right (Figure 6C), and from 1.33 to 2.26±0.16 mm on the left (Figure 6D), in accordance with the logarithmic functions: $y = -5.014 + 2.176 \times \ln(\text{Age}) \pm 0.218$ ($R^2 = 0.72$) and $y = -5.624 + 3.43 \times \ln(\text{Age}) \pm 0.197$ ($R^2 = 0.77$), respectively. The cross-sectional area of the neural ossification centers rose from 2.70 to 12.23±3.68 mm² on the right (Figure 7A) and from 2.60 to 11.93±4.03 mm² on the left (Figure 7B), like the linear functions: $y = -12.122 + 0.847 \times \text{Age} \pm 1.351$ ($R^2 = 0.82$) and $y = -11.828 + 0.798 \times \text{Age} \pm 1.336$ ($R^2 = 0.81$), respectively. The volumetric growth of the right (Figure 7C) and left (Figure 7D) neural ossification centers ranged from 8.89 to 14.61±4.94 mm³, and from 3.64 to 15.10±4.89 mm³, respectively, according to the linear functions $y = -10.902 + 0.854$

$\times \text{Age} \pm 2.141$ ($R^2 = 0.68$), and $y = -13.205 + 0.936 \times \text{Age} + 1.603$ ($R^2 = 0.81$), respectively.

Discussion

Early mineralization stages of vertebral ossification centers can be visualized histologically from the 10th week of gestation [29], before its radiographic [18] or echographic [30,31] recognition. Some authors using roentgenographic [32] and ultrasonographic [30,33] methods confirmed the influence of sex on timing of appearance of ossification centers within the fetal spine, being significantly earlier in females than in males. According to Vignolo et al. [33], the percentage of appearance of sacral ossification centers in females was significantly ($P = 0.019$) higher than in males at every week of gestation. In fetuses aged 21 weeks, ossification centers of S5 vertebra were visualized in its body and neural processes in 42.9% and in 28.6% of the females, respectively, and in none of the males. Thus, visualization of vertebral ossification centers in clinical practice may be impeded in male fetuses during early pregnancy [33]. Furthermore, in fetuses aged 11–14 weeks, the spinal length, expressed as z-score, was significantly ($P = 0.008$)

Table 4. Morphometric parameters of ossification centers of neural processes of L3 vertebra.

Age (weeks)	n	Right neural arch							
		Length (mm)		Width (mm)		Cross-sectional area (mm ²)		Volume (mm ³)	
		mean	SD	mean	SD	mean	SD	mean	SD
17	1	2.56		1.15		2.70		8.89	
18	3	3.63	1.08	1.37	0.11	5.40	1.73	5.97	1.14
19	8	2.63	0.36	1.30	0.18	3.44	0.66	4.37	0.67
20	4	↓ (P<0.01) 3.21	0.06	↓ (P<0.01) 1.65	0.24	↓ (P<0.01) 4.75	0.70	↓ (P<0.01) 5.56	1.11
21	4	4.32	0.73	4.32	0.06	5.40	1.34	6.89	1.68
22	4	4.12	0.16	1.84	0.27	6.75	0.78	7.51	1.33
23	5	↓ (P<0.01) 4.58	0.58	↓ (P<0.05) 1.90	0.23	↓ (P<0.01) 7.78	1.79	↓ (P<0.01) 8.90	1.92
24	9	4.41	0.52	1.94	0.21	7.71	1.12	9.06	1.57
25	1	3.65		1.82		7.00		7.97	
26	2	↓ (P<0.001) 6.24	0.42	↓ (P<0.01) 2.16	0.06	↓ (P<0.001) 11.36	0.64	↓ (P<0.001) 18.25	7.56
27	6	5.44	1.16	2.04	0.41	10.06	3.38	14.09	5.97
28	2	6.61	2.00	2.07	0.18	13.40	0.14	14.60	2.40
29	2	↓ (P<0.05) 5.54	0.02	↓ (P<0.01) 2.33	0.10	↓ (P<0.01) 9.75	0.07	↓ (P<0.01) 11.20	0.24
30	4	5.88	0.66	2.32	0.23	12.23	3.68	14.61	4.94
Age (weeks)	n	Left neural arch							
		Length (mm)		Width (mm)		Cross-sectional area (mm ²)		Volume (mm ³)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
17	1	2.34		1.33		2.60		3.64	
18	3	3.70	1.65	1.49	0.38	6.93	3.32	7.93	3.22
19	8	2.21	0.45	1.25	0.13	3.23	0.82	4.13	0.87
20	4	↓ (P<0.01) 3.27	0.13	↓ (P<0.05) 1.31	0.20	↓ (P<0.01) 3.98	0.77	↓ (P<0.01) 5.35	0.94
21	4	3.53	0.04	1.40	0.07	3.45	0.58	6.38	1.08
22	4	4.69	0.63	1.72	0.24	6.78	0.60	7.74	0.75
23	5	↓ (P<0.01) 4.54	0.78	↓ (P<0.05) 1.85	0.26	↓ (P<0.001) 6.86	1.92	↓ (P<0.001) 8.34	1.75
24	9	4.30	0.65	1.73	0.18	6.90	1.32	9.37	2.10
25	1	3.18		1.34		5.90		8.23	
26	2	↓ (P<0.001) 6.28	0.05	↓ (P<0.001) 2.32	0.13	↓ (P<0.001) 9.80	0.14	↓ (P<0.001) 16.75	7.14
27	6	5.60	1.02	2.01	0.29	9.70	2.87	13.24	5.58
28	2	7.42	0.01	2.24	0.28	11.50	1.27	14.85	3.04
29	2	↓ (P<0.01) 5.76	0.01	↓ (P<0.05) 2.22	0.01	↓ (P<0.01) 11.40	0.28	↓ (P<0.01) 12.95	0.21
30	4	5.90	0.80	2.26	0.16	11.93	4.03	15.10	4.89

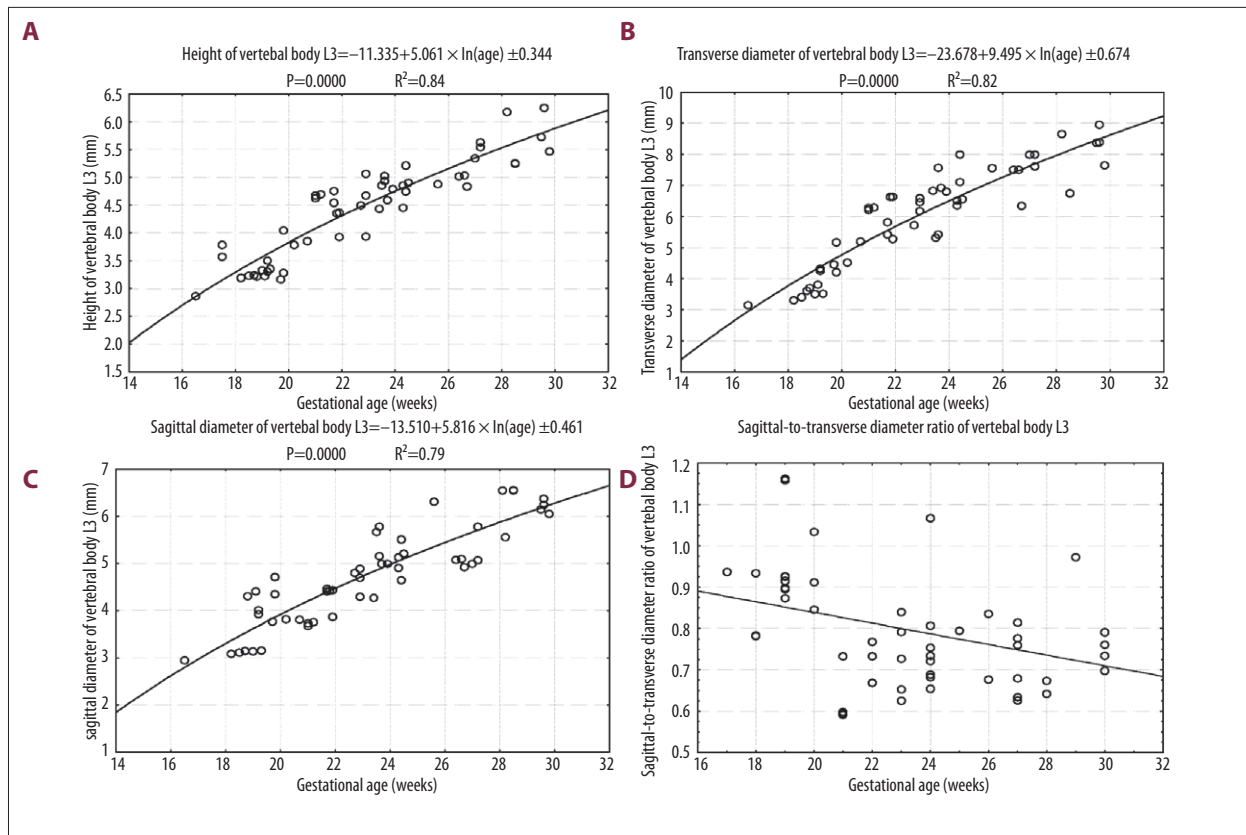


Figure 2. Regression lines for height (A), transverse diameter (B), sagittal diameter (C), and sagittal-to-transverse diameter ratio (D) of the L3 vertebral body.

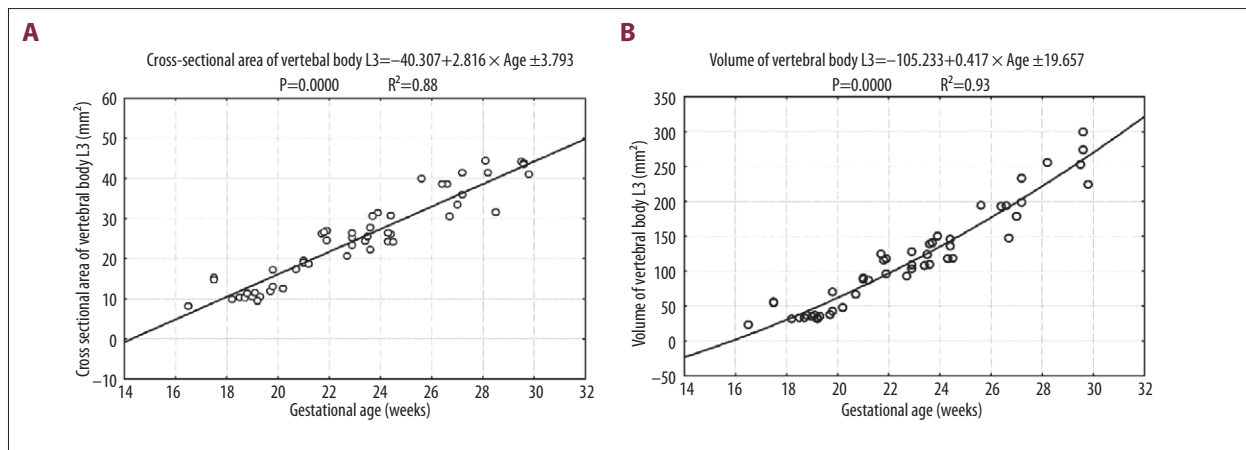


Figure 3. Regression lines for cross-sectional area (A) and volume (B) of the L3 vertebral body.

larger in females (0.12 ± 0.76) than in males (-0.37 ± 0.84). In this aspect our results do not correspond with the medical literature, because a lack of statistically significant sex differences for all the parameters of the fetal spine was found in the present study.

Growth dynamics of the lumbar spine length have previously been reported to be linear [21,22], quadratic [13], or

exponential [23] with gestational ages. According to Shin et al. [24], the height of L1 vertebra increased linearly from 3.8 ± 0.3 to 7.1 ± 0.4 mm for the 26-week and 41-week groups of gestation, respectively. During that time the mean weekly increment in the height of L1 vertebra was 0.23 mm in males and 0.20 mm in females. However, the height of the L1 vertebra: body length ratio progressively increased with age, from 0.012 in fetuses aged 26–30 weeks to 0.014 in fetuses aged 36–41

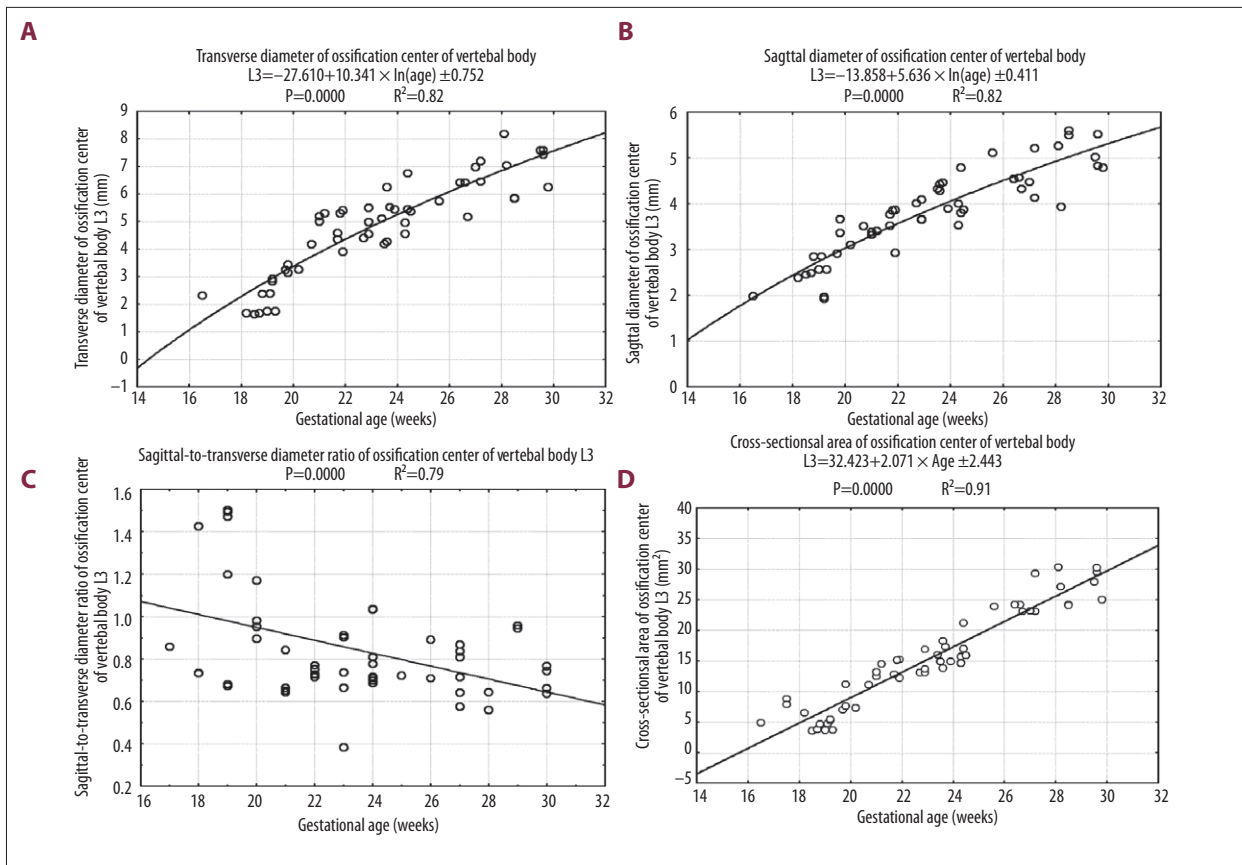


Figure 4. Regression lines for transverse diameter (A), sagittal diameter (B), sagittal-to-transverse diameter ratio (C), and cross-sectional area (D) of the ossification center of the L3 vertebral body.

weeks, with a growth spurt in L1 vertebra at 34 weeks of gestation. Bagnall et al. [13] showed that in fetuses aged 8–26 weeks the lumbar spine length was represented by the quadratic function $y = -16.11 + 133.83 \times \text{Age} - 69.93 \times \text{Age}^2$ (Age – in years), with a negative coefficient of the power 2, indicating a gradually decreasing rate of growth. Furthermore, the length of the “average” lumbar unit (vertebra plus disc) at 26 weeks of gestation reached the value of 6.8 mm. For the lumbar spine length, the exponential function $y = \exp(4.705 - 32.4/\text{Age})$ [23] was much better ($R^2 = 0.959$ vs. $R^2 = 0.865$; $P < 0.01$) than the linear function $y = -10.85 + 1.627 \times \text{Age}$ [17].

In the present study, the 3 main measurements (height, and transverse and sagittal diameters) of the L3 vertebral body did not form linear, quadratic, or exponential functions on nomograms. The best-fit growth models for them were the following logarithmic functions: $y = -11.335 + 5.061 \times \ln(\text{Age}) \pm 0.344$ for its height, $y = -23.678 + 9.495 \times \ln(\text{Age}) \pm 0.674$ for its transverse diameter, and $y = -13.510 + 5.816 \times \ln(\text{Age}) \pm 0.461$ for its sagittal diameter. Thus, their growth velocity was gradually decreasing with age, in agreement with results of Bagnall et al. [13]. Of note, the vertebral body did not reveal a proportionate evolution, because the sagittal -to- transverse diameter

ratio showed a significant decrease in values from 0.88 ± 0.11 to 0.71 ± 0.08 during the study period. Since both the transverse and sagittal diameters of the vertebral body increased logarithmically, its cross-sectional area, being approximately a product of these 2 diameters, followed according to the linear fashion $y = -40.307 + 2.816 \times \text{Age} \pm 3.793$, thereby providing the medical literature with completely novel data.

Schild et al. [23] demonstrated 3-dimensional sonographic volume calculation of the L1 and L5 vertebral bodies, and the whole lumbar spine in the 16–37 week fetus. The volumetric growth of the vertebral bodies followed according to exponential functions. The growth in volume of L1, L5 and L1–5 vertebrae ranged from 0.049 to 2.626 ml, from 0.033 to 2.121 ml, and from 0.364 to 14.417 ml, respectively, in accordance ($P < 0.01$) with the following exponential functions: $y = \exp(2.99 - 89.76/\text{Age})$ for L1 vertebra ($R^2 = 0.92$), $y = \exp(2.74 - 90.81/\text{Age})$ for L5 vertebra ($R^2 = 0.90$), and $y = \exp(4.94 - 89.81/\text{Age})$ for L1–5 vertebrae ($R^2 = 0.94$). In the material under examination, the vertebral body volume varied from 23.17 to $262.47 \pm 32.04 \text{ mm}^3$, being modeled as the quadratic function $y = -105.233 + 0.417 \times \text{Age}^2 \pm 19.657$. In our opinion, the best volumetric model expressed by the quadratic function probably resulted from multiplying

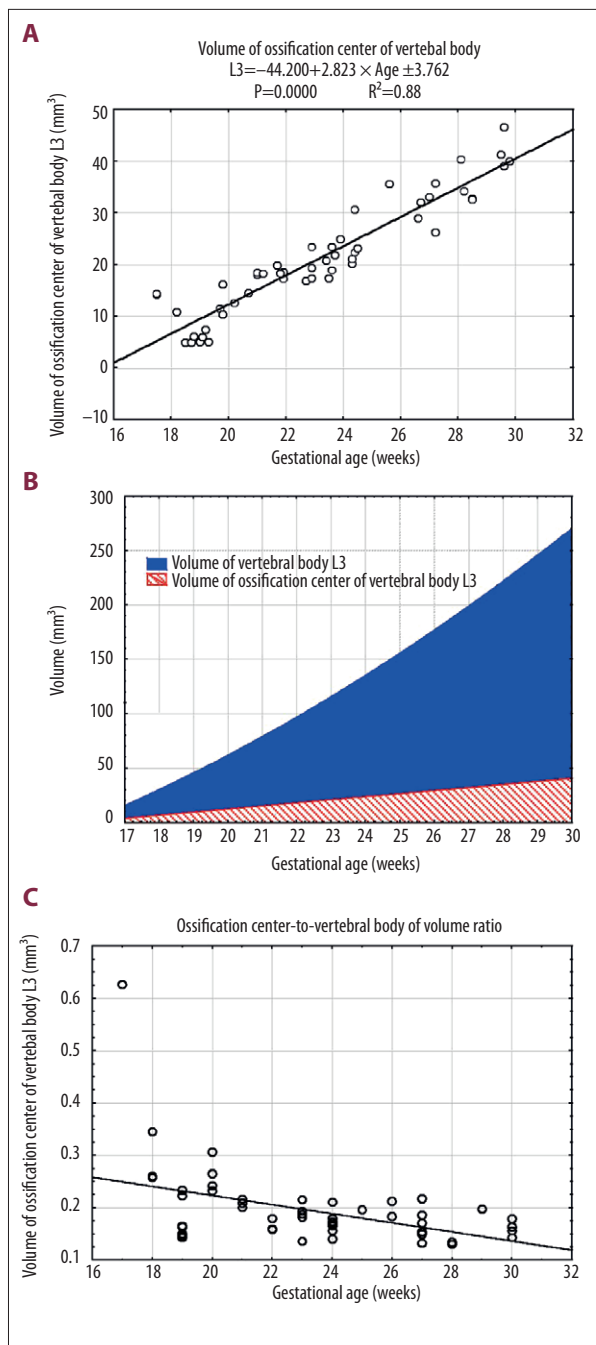


Figure 5. Regression lines for volume of the ossification center of the L3 vertebral body (A), when compared to volume of the L3 vertebral body (B), and the ossification center-to-vertebral body volume ratio (C).

the 3 values for height, and transverse and sagittal diameters, each changing logarithmically. Baumgart et al. [26] reported that the C4 vertebral body increased logarithmically in height and sagittal and transverse diameters, linearly in cross-sectional area, and 4-degree polynomially in volume. According to Szpinda et al. [25], in the human fetus the vertebral body is

characterized by maximum values in sagittal diameter for T7, in transverse diameter for L1, in height for L2, and in cross-sectional area and volume for L3.

After reviewing the medical literature on vertebral ossification centers [13,16,18–20,29,32,33], we found only 2 original articles providing us with reference data for their dimensions [26,27]. As reported by Baumgart et al. [26], the 3 ossification centers of C4 vertebra grew logarithmically in transverse and sagittal diameters, and linearly in cross-sectional area and volume. According to Szpinda et al. [27], the body ossification center attained maximum values in transverse diameter for L1–L3 vertebrae, in sagittal diameter for T6–T9 vertebrae, in cross-sectional area for L2 vertebra, and in volume for L3 vertebra. Therefore, the present CT, digital, and statistical study is the first to provide reference values and growth dynamics for length, width, cross-sectional area, and volume of the 3 ossification centers of L3 vertebra in normal human fetuses.

As illustrated in Tables 3 and 4 and Figure 8, the ossification center of the L3 vertebral body was much larger than that of each neural process. However, the growth dynamics for the 3 ossification centers of the L3 vertebra were all alike. Both their transverse and sagittal diameters increased logarithmically, whereas their cross-sectional areas and volumes followed proportionately. Interestingly, the vertebral body and its ossification center grew in volume according to the quadratic ($y = -105.233 + 0.417 \times \text{Age}^2 \pm 19.657$) and linear ($y = -44.200 + 2.823 \times \text{Age} \pm 3.762$) functions, respectively. Thus, the relative size of the ossification center gradually decreased with age, from 0.24 ± 0.06 at 17 weeks to 0.14 ± 0.05 at 30 weeks of gestation. As far as the neural processes are concerned, their left and right ossification centers developed symmetrically, with no laterality differences.

On the basis of age-specific reference values for L3 vertebra such fetal spinal abnormalities as lumbosacral agenesis, hemivertebra and spina bifida may ultrasonographically be diagnosed and monitored in utero. Lumbosacral agenesis may refer to partial or total unilateral (type I) or bilaterally symmetrical (type II) defect of the sacrum, and to absence of the sacrum and various lumbar vertebrae, the lowest of which articulates with the iliac ilia (type III) or only rests above them [34]. Hemivertebra is characterized by a laterally-based wedge vertebra with unilateral aplasia of one of the paired chondrification centers within the vertebral body, a single pedicle, and hemilamina, causing scoliosis, lordosis, or kyphosis [8–11,35]. Hemivertebra is commonly associated with other skeletal anomalies [10], diastematomyelia [36], cardiac, urogenital, and gastrointestinal tract anomalies [8], and some syndromes, including Jarcho-Levin syndrome, Klippel-Fiel syndrome, VATER syndrome (vertebral anomalies, imperforate anus, tracheo-esophageal fistula, renal anomalies), VACTERL syndrome (VATER, cardiac and

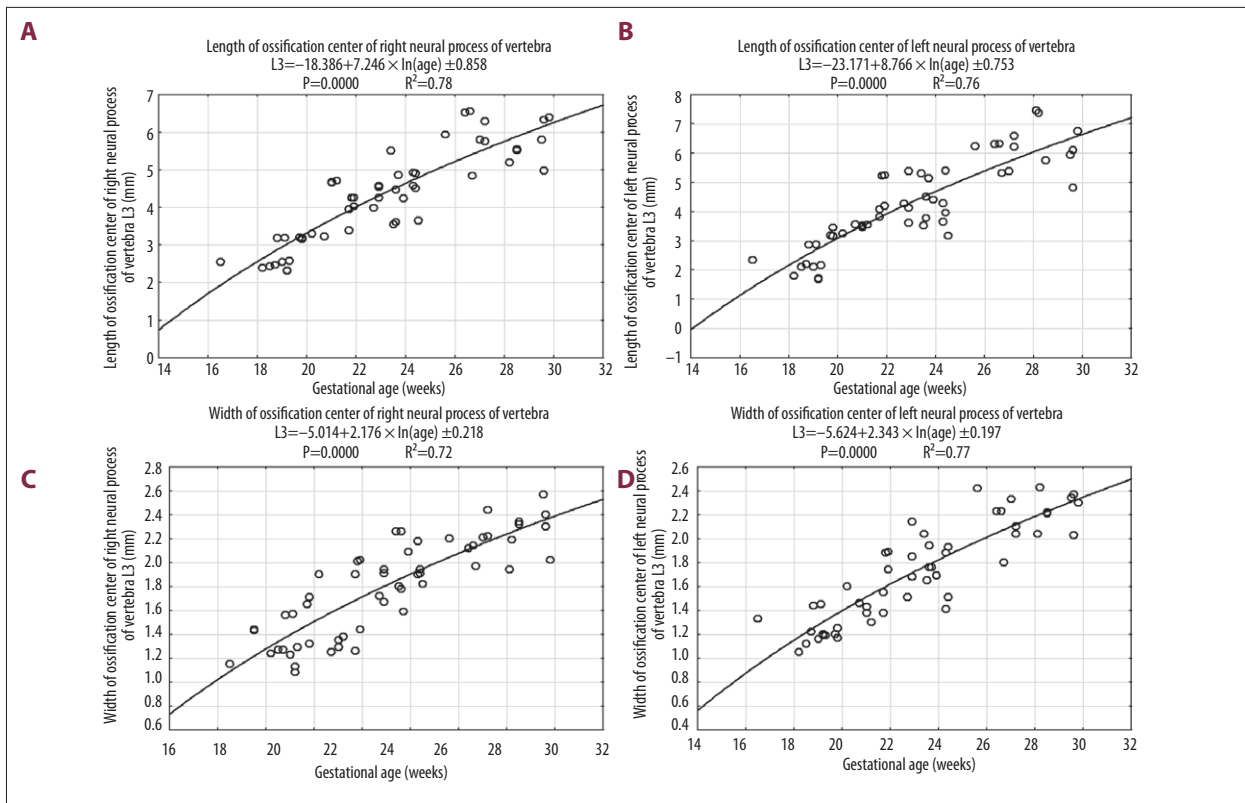


Figure 6. Regression lines for length on the right (A) and left (B) and for width on the right (C) and left (D) of the neural processes.

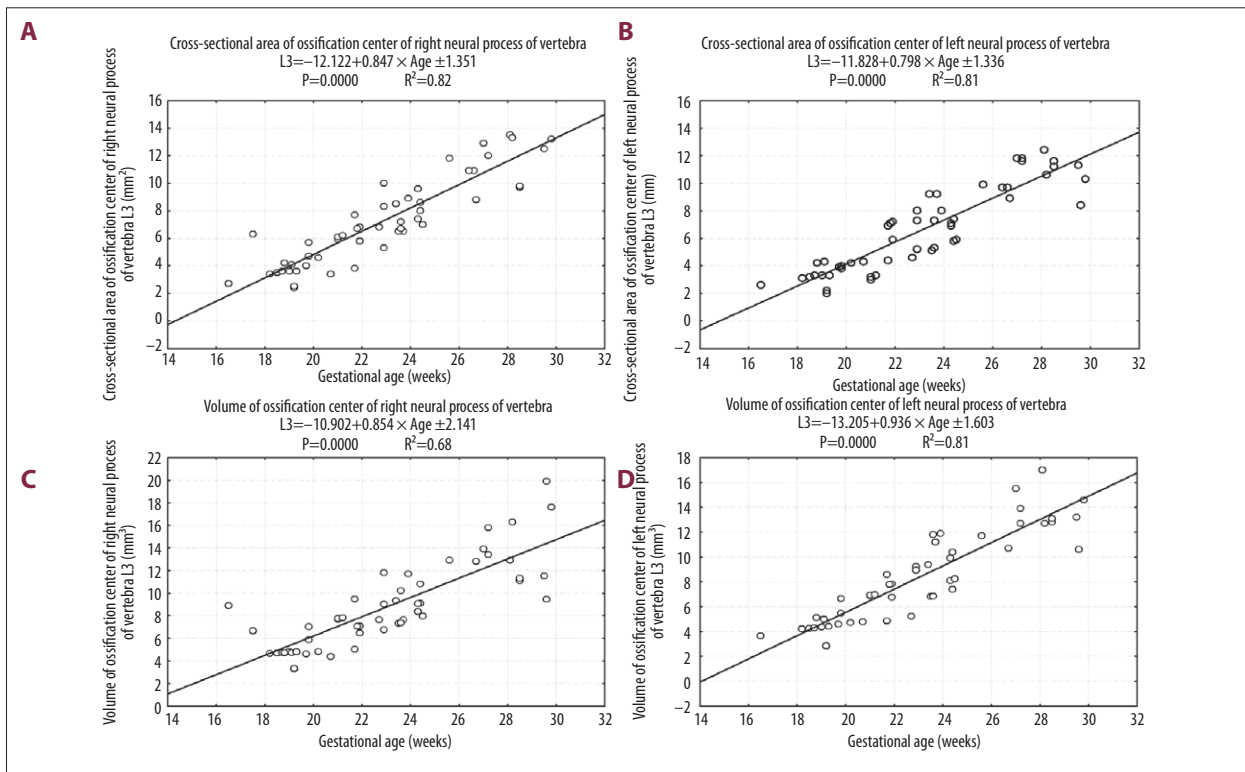


Figure 7. Regression lines for cross-sectional area on the right (A) and left (B) and for volume on the right (C) and left (D) of the neural processes.

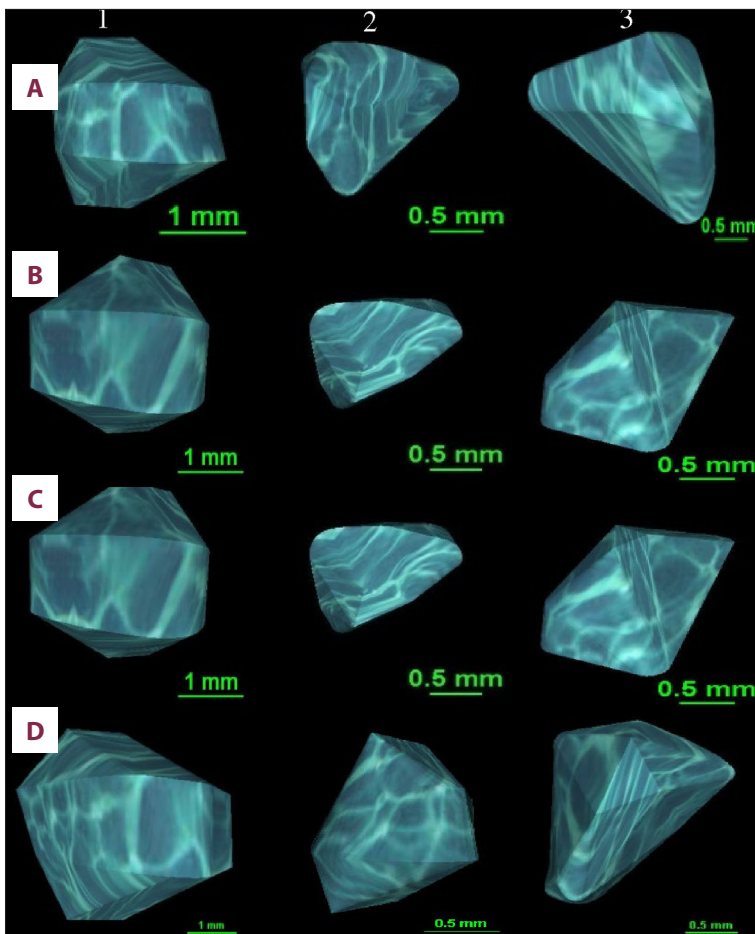


Figure 8. Ossification centers of the L3 vertebral body (1), right (2) and left (3) neural processes of L3 vertebra in fetuses aged 17 weeks (A), 22 weeks (B), 26 weeks (C), and 30 weeks (D).

limb anomalies), OEIS (omphalocele, urinary bladder exstrophy, imperforate anus, and spinal anomalies), the Potter sequence, and spina bifida [11,35]. The most relevant form of spina bifida is myelomeningocele with the unfused neural processes of the lumbosacral spine, allowing the spinal cord to protrude through an opening [37,38]. Furthermore, detailed knowledge of the growth of vertebral ossification centers in the fetal period may be helpful in the prenatal detection of skeletal dysplasias (osteochondrodysplasias) resulting in a delay in appearance of ossification centers and poor mineralization, which is typical of osteogenesis imperfecta type II [12,39], achondrogenesis [40], thanatophoric dysplasia type I [12], and hypophosphatasia [41].

The present study provides completely novel, accurate data on dimensions of the L3 vertebra and its 3 ossification centers at varying gestational ages, which may be potentially useful in clinical practice.

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Conclusions

1. No sex differences are found in the morphometric parameters of the L3 vertebra and its 3 ossification centers.
2. The growth dynamics of the L3 vertebral body follow logarithmically for its height, and sagittal and transverse diameters, linearly for its cross-sectional area, and quadratically for its volume.
3. The growth dynamics of the 3 ossification centers of the L3 vertebra follow logarithmically in their transverse and sagittal diameters, and linearly in their cross-sectional area and volume.
4. The age-specific reference intervals of the L3 vertebra and its 3 ossification centers present the normative values of clinical importance in the diagnosis of congenital spinal defects.

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