Cross-sectional study of C1–S5 vertebral bodies in human fetuses

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Abstract

Introduction: Knowledge on the normative spinal growth is relevant in the prenatal detection of its abnormalities. The present study determines the height, transverse and sagittal diameters, cross sectional area, and volume of individual C1–S5 vertebral bodies.
Material and methods: Using the methods of computed tomography (CT), digital image analysis, and statistics, the size of C1–S5 vertebral bodies in 55 spontaneously aborted human fetuses aged 17–30 weeks was examined.
Results: All the 5 examined parameters changed significantly with gestational age ($p < 0.01$). The mean height of vertebral bodies revealed an increase from the atlas (2.39 ±0.54 mm) to L2 (4.62 ±0.97 mm), stabilized through L3–L4 (4.58 ±0.92 mm, 4.61 ±0.84 mm), and then was decreasing to S5 (0.43 ±1.06 mm). The mean transverse diameter of vertebral bodies was increasing from the atlas (1.20 ±1.96 mm) to L1 (6.24 ±1.46 mm), so as to stabilize through L2–L3 (6.12 ±1.65, 6.12 ±1.61 mm), and finally was decreasing to S5 (0.26 ±0.96 mm). There was an increase in sagittal diameter of vertebral bodies from the atlas (0.82 ±1.34 mm) to T7 (4.76 ±0.85 mm), its stabilization for T8–L4 (4.73 ±0.86 mm, 4.71 ±1.02 mm), and then a decrease in values to S5 (0.21 ±0.75 mm) was observed. The values for cross-sectional area of vertebral bodies were increasing from the atlas (2.95 ±5.25 mm^2) to L3 (24.92 ±11.07 mm^2), and then started decreasing to S5 (0.48 ±2.09 mm^2). The volumetric growth of vertebral bodies was increasing from the atlas (8.60 ±16.40 mm^3) to L3 (122.16 ±74.73 mm^3), and then was decreasing to S5 (1.60 ±7.00 mm^3).
Conclusions: There is a sharp increase in size of fetal vertebral bodies between the atlas and the axis, and a sharp decrease in size within the sacral spine. In human fetuses the vertebral body growth is characterized by maximum values in sagittal diameter for T7, in transverse diameter for L1, in height for L2, and in both cross-sectional area and volume for L3.

Key words: vertebral body, dimensions, computed tomography examination, digital image analysis, human fetuses.

Introduction

The evaluation of the fetal spine in both horizontal and parasagittal projections is of great relevance in routine ultrasonography after the 12th week of pregnancy [1, 2]. As a result, most fetal structures *in utero* can be examined and commented on both in normal and pathological conditions [1, 3–9]. Detailed knowledge is a prerequisite for both the prenatal diagnosis and exclusion of many structural spinal abnormalities such as achondrogenesis [10], caudal regression syndrome [11], hemivertebra [12–16], butterfly vertebra [17], and hypophosphatasia [18], which are responsible for longitudinal growth imbalance. Although Dimeglio and Bonnel [19] believed that the fetal spine had only one primary curvature, a global kyphosis extending from cranial to caudal, some authors proved the presence of secondary curvatures, both cervical [20] and lumbar [2] lordoses.

The heights of the cervical, thoracic, lumbar and sacral vertebral bodies in fetuses are in the following proportions to each other: 1/2 : 3/4 : 1 : 2/5, respectively [21]. To date however, vertebral body heights excepted, there has been no information on the quantitative analysis of the transverse and sagittal diameters, cross-sectional areas, and volumes of vertebral bodies. In order to address this question in considerable detail, in this study we aimed: to determine the height, transverse and sagittal diameters, cross sectional area, and volume of the individual C1–S5 vertebral bodies, to display graphically the relative growth of each parameter for the individual vertebrae.

Material and methods

Material

This study included 55 ethnically homogeneous human fetuses (27 males, 28 females) of Caucasian racial origin at ages of 17–30 weeks (Table I), which had been derived from spontaneous abortions or stillbirths in the years 1989–2001 as a result of placental insufficiency. Gestational ages were estimated by the crown-rump length (CRL) [22] and known date of the beginning of the last maternal menstrual period. The use of the fetuses for research was accepted by our University Research Ethics Committee (KB 275/2011). On macroscopic examination both internal and external anatomical malformations, including those related to chromosomal disorders, were ruled out in all included specimens, which were diagnosed as normal. Furthermore, the fetuses studied could not suffer from growth retardation, because the correlation between the gestational age based on the CRL and that calculated by the last menstruation attained the value $r = 0.98$ ($p < 0.001$).

Measurements

After having been fixed in 10% neutral buffered formalin solution, every fetus underwent a computed tomography (CT) examination with both the reconstructed slice width option of 0.4 mm and the number of 128 slices acquired simultaneously by Biograph mCT (Siemens). No spine showed evidence of maldevelopment. The scans obtained were stored in DICOM formats (Figure 1 A), so as both to compute three-dimensional reconstructions and to perform the morphometric analysis of chosen objects. Next DICOM formats were evaluated by digital image analysis of Osirix 3.9, which semi-automatically estimated linear (sagittal and transverse diameters), two-dimensional (cross-sectional area), and three-dimensional (volume) parameters of the

Table I. 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

The gestational age based on the CRL and that calculated by the known date of the beginning of the last maternal menstrual period were highly correlated ($R = 0.98$; $p < 0.001$).

Figure 1. CT of a male fetus aged 25 weeks (in the sagittal projection) recorded in DICOM formats (**A**) with vertebral bodies (in the transverse projection) of C4 (**B**), T6 (**C**), and L3 (**D**), assessed by Osirix 3.9

C1–S5 vertebral bodies (Figures 1 B–D, 2 A, B). The contouring procedure for each vertebral body was outlined with a cursor and recorded.

For each individual, the following 5 features of the C1–S5 vertebral bodies were assessed:
1) height (in mm), corresponding to the distance between the superior and inferior borderlines of the vertebral body (in sagittal projection),
2) transverse diameter (in mm), corresponding to the distance between the left and right borderlines of the vertebral body (in transverse projection),
3) sagittal diameter (in mm), corresponding to the distance between the anterior and posterior borderlines of the vertebral body (in sagittal projection),
4) cross-sectional area (in mm^2), traced around the vertebral body (in transverse projection), and
5) volume (in mm^3).

In a continuous effort to minimize measurements and observer bias, all the measurements were done by the same researcher (M.B.). Each measurement was made 3 times under the same conditions but at different times, and the mean of the three was finally accepted. The 7975 individual results for the whole material were subjected to statistical analysis.

Statistical analysis

The intra-observer variation was assessed by the Wilcoxon signed-rank test. The data obtained were checked for normality of distribution using the Kolmogorov-Smirnov test and homogeneity of variance using Levene's test. For statistics, the sample was separated into 4 age cohorts: group I (17–19 weeks) 12 specimens, group II (20–23 weeks) 17 specimens, group III (24–27 weeks) 18 specimens, and group IV (28–30 weeks) 8 specimens. As the next step of the statistical analysis, Student's *t*-test was used to examine whether sex influenced the values obtained. After checking possible sex differences between the 4 afore-mentioned age groups, we tested them for the entire group, without taking into account fetal ages. To check whether significant differences existed with age, the one-way ANOVA test and *post-hoc* Turkey's test were used for the 4 age groups. By plotting the numerical data of each vertebral body parameter versus the corresponding vertebra we obtained specific curves for the C1–S5 vertebral bodies.

Results

In the examined material all the C1–S5 vertebral bodies were identified. Furthermore, every fetal spine was characterized by two primary curvatures (thoracic and sacral kyphoses) and two well-pronounced secondary curvatures (cervical and lumbar lordoses) (Figures 1 A, 2 A).

Insignificant differences were observed in the evaluation of intra-observer reproducibility of the spinal measurements. In addition, since no significant difference was observed in the values of the parameters studied according to sex, no attempt was made to further separate the results obtained according to sex. By contrast, advancing gestational age was characterized by a statistically significant ($p < 0.01$) change in values of all the measurements in the 4 aforementioned groups.

Computed tomography images of fetuses in the sagittal projection for every gestational week are presented as follows: Figures 3 A–D for the age of 17–20 weeks, Figures 4 A–D for the age of 21–24 weeks, Figures 5 A–D for the age of 25–28 weeks, and Figures 6 A, B for the age of 29–30 weeks. The following 5 figures display the patterns for growth in height (Figure 7), transverse diameter (Figure 8), sagittal diameter (Figure 9), cross-sectional area (Figure 10), and volume (Figure 11) of the C1–S5 vertebral bodies in fetuses at ages of 17–19, 20–23, 24–27 and 28–30 weeks. The mean values for the whole group are presented in Table II. The growth dynamics for each parameter was similar in the 4 particular age groups. In all, the values for the atlas were much smaller than for the axis, being expressed by the following means: 2.39 ±0.54 mm vs. 2.92 ±0.46 mm for height, 1.20 ±1.96 mm vs. 3.98 ±0.86 mm for transverse diameter, 0.82 ±1.34 mm vs. 3.07 ±0.60 mm for sagittal diameter, 2.95 ±5.25 mm^2 vs. 10.88 ±4.33 mm^2 for cross-sectional area, and 8.60 ±16.40 mm^3 vs. 33.12 ±17.68 mm^3 for volume.

The mean height of vertebral bodies revealed a gradual increase from the axis (2.92 ±0.46 mm) to vertebra L2 (4.62 ±0.97 mm), stabilized through vertebrae L3 (4.58 ±0.92 mm) and L4 (4.61 ±0.84 mm), and decreased from vertebra L5 (4.50 ±0.93 mm) to vertebra S5 (0.43 ±1.06 mm).

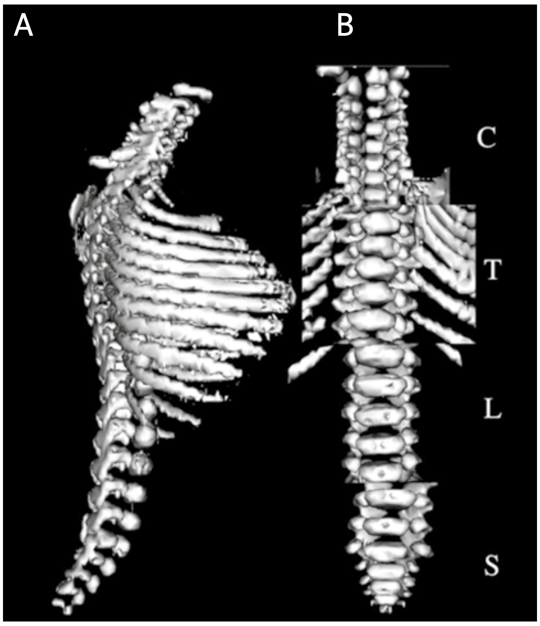

Figure 2. Reconstruction of the spine in the lateral (**A**) and anterior (**B**) projections in a female fetus aged 27 weeks
C – cervical part, T – thoracic part, L – lumbar part, S – sacral part.

The mean transverse diameter of vertebral bodies gradually increased from the axis (3.98 ±0.86 mm) to vertebra L1 (6.24 ±1.46 mm), so as to stabilize through vertebrae L2 (6.12 ±1.65 mm) and L3 (6.12 ±1.61 mm), and finally decreased to reach the value of 0.26 ±0.96 mm for vertebra S5. The values for vertebrae L5 (5.36 ±1.48 mm) and T2–T4 (5.34 ±1.19 mm, 5.37 ±0.98 mm, 5.35 ±0.93 mm, respectively) were approximately equivalent.

There was a gradual increase in the sagittal diameter of vertebral bodies from the axis (3.07 ±0.60 mm) to vertebra T7 (4.76 ±0.85 mm), and its stabilization for vertebrae T8 (4.73 ±0.86 mm) – L4 (4.71 ±1.02 mm). A decrement in values from 4.40 ±1.12 mm for vertebra L5 to 0.21 ±0.75 mm for vertebra S5 was observed afterwards. The values for vertebrae S1 (3.49 ±1.86 mm) and C5 (3.48 ±0.51 mm), and for L5 (4.40 ±1.12 mm) and T3 (4.44 ±0.75 mm) were approximately equivalent.

The values for cross-sectional area of vertebral bodies gradually increased from the axis (10.88 ±4.33 mm^2) to vertebra L3 (24.92 ±11.07 mm^2), and then started declining to reach the value of 0.48 ±2.09 mm^2 for vertebra S5. The cross-sectional areas of the following vertebral bodies were approximately equivalent to each other: S2 (11.18 ±9.05 mm^2) and C2–C4 (10.88 ±4.33 mm^2, 10.79 ±4.29 mm^2, and 11.36 ±3.40 mm^2), L5 (21.32 ±11.04 mm^2), T9 (21.31 ±7.64 mm^2) and T10 (21.30 ±7.32 mm^2).

The volumetric growth of vertebral bodies gradually increased from the axis (33.12 ±17.68 mm^3) to vertebra L3 (122.16 ±74.73 mm^3). Next, there was a gradual decrease in their volumes from vertebra

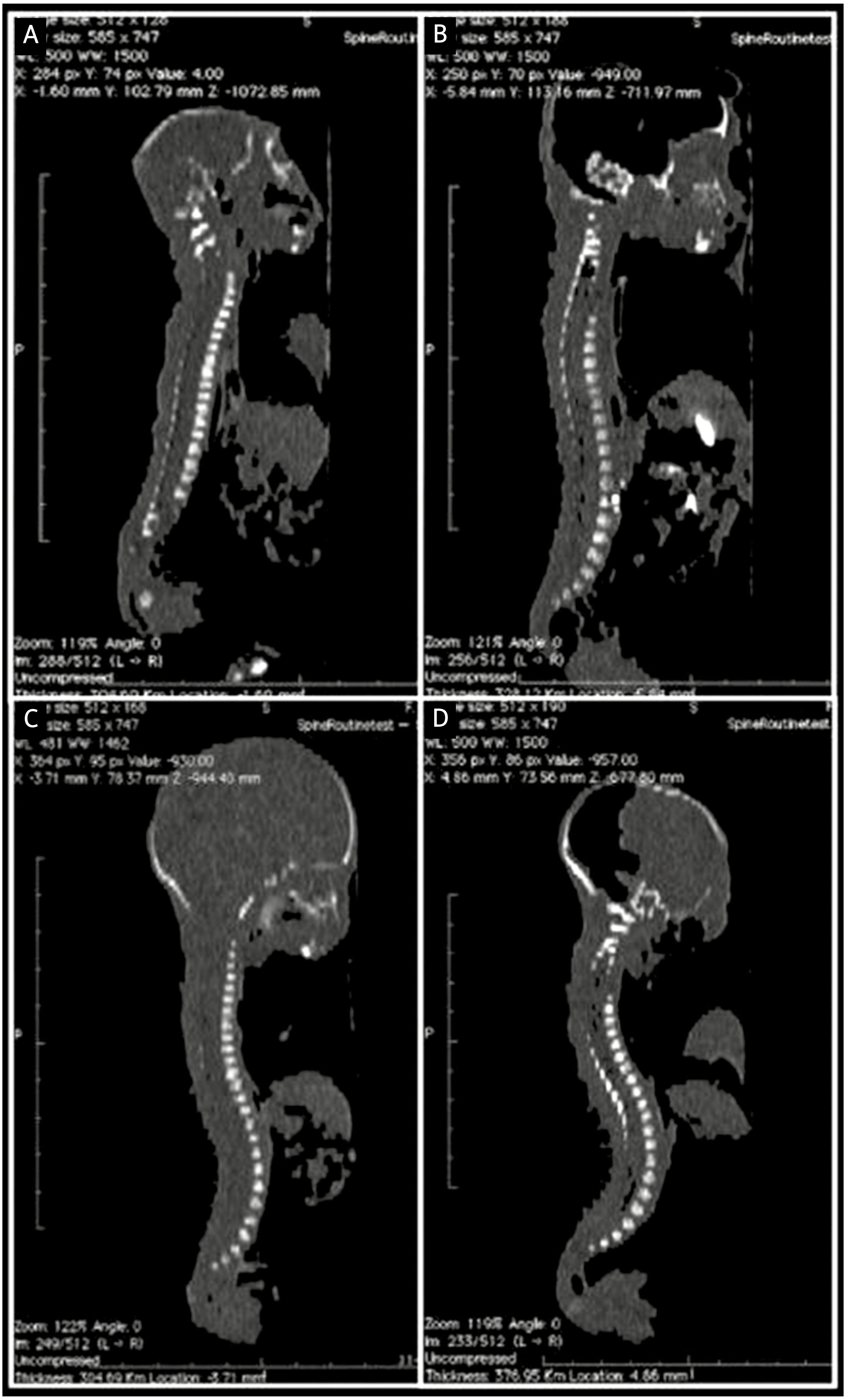

Figure 3. CT images of fetuses aged 17 (**A**), 18 (**B**), 19 (**C**), and 20 (**D**) weeks in the sagittal projection recorded in DICOM formats

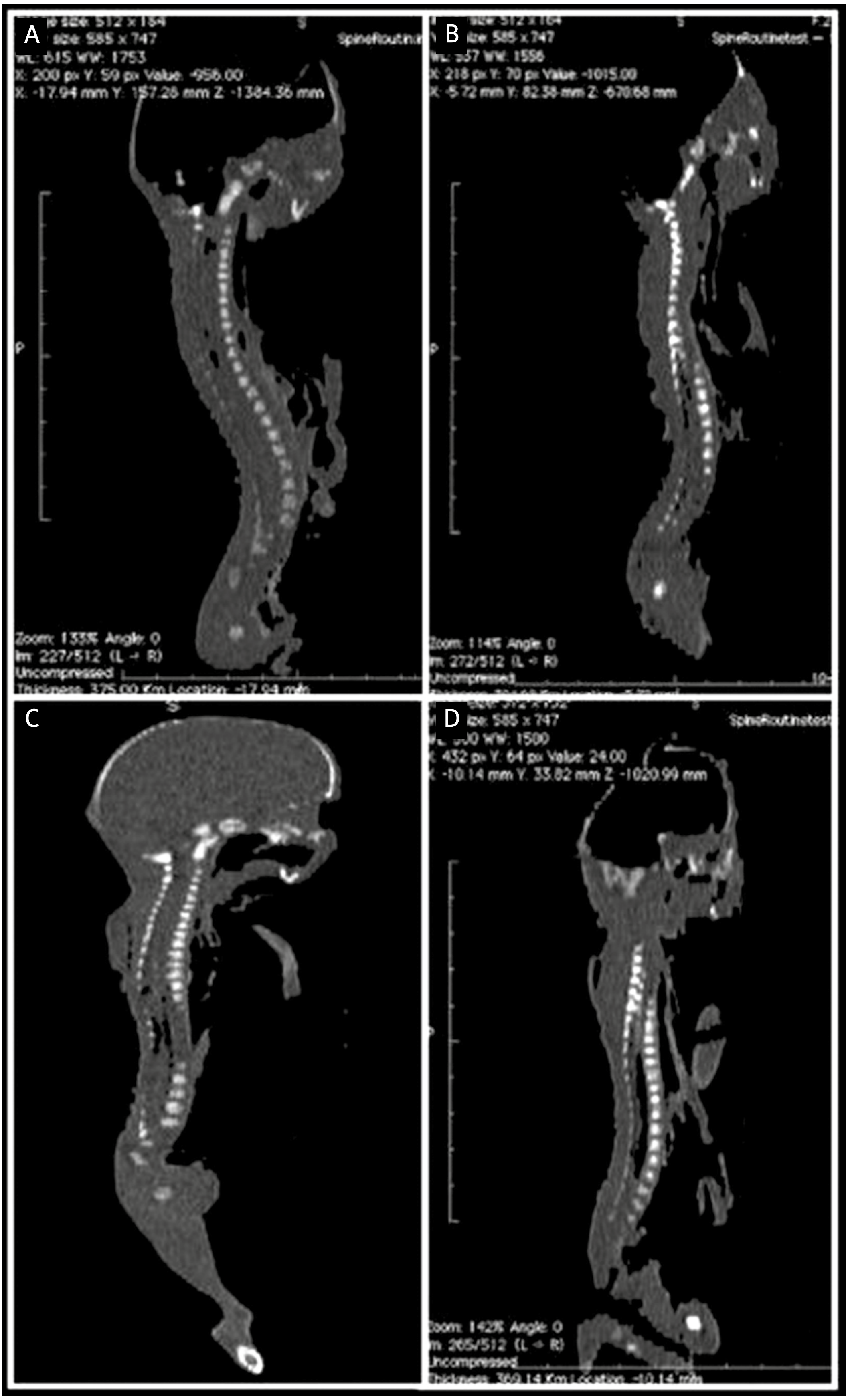

Figure 4. CT images of fetuses aged 21 (**A**), 22 (**B**), 23 (**C**), and 24 (**D**) weeks in the sagittal projection recorded in DICOM formats

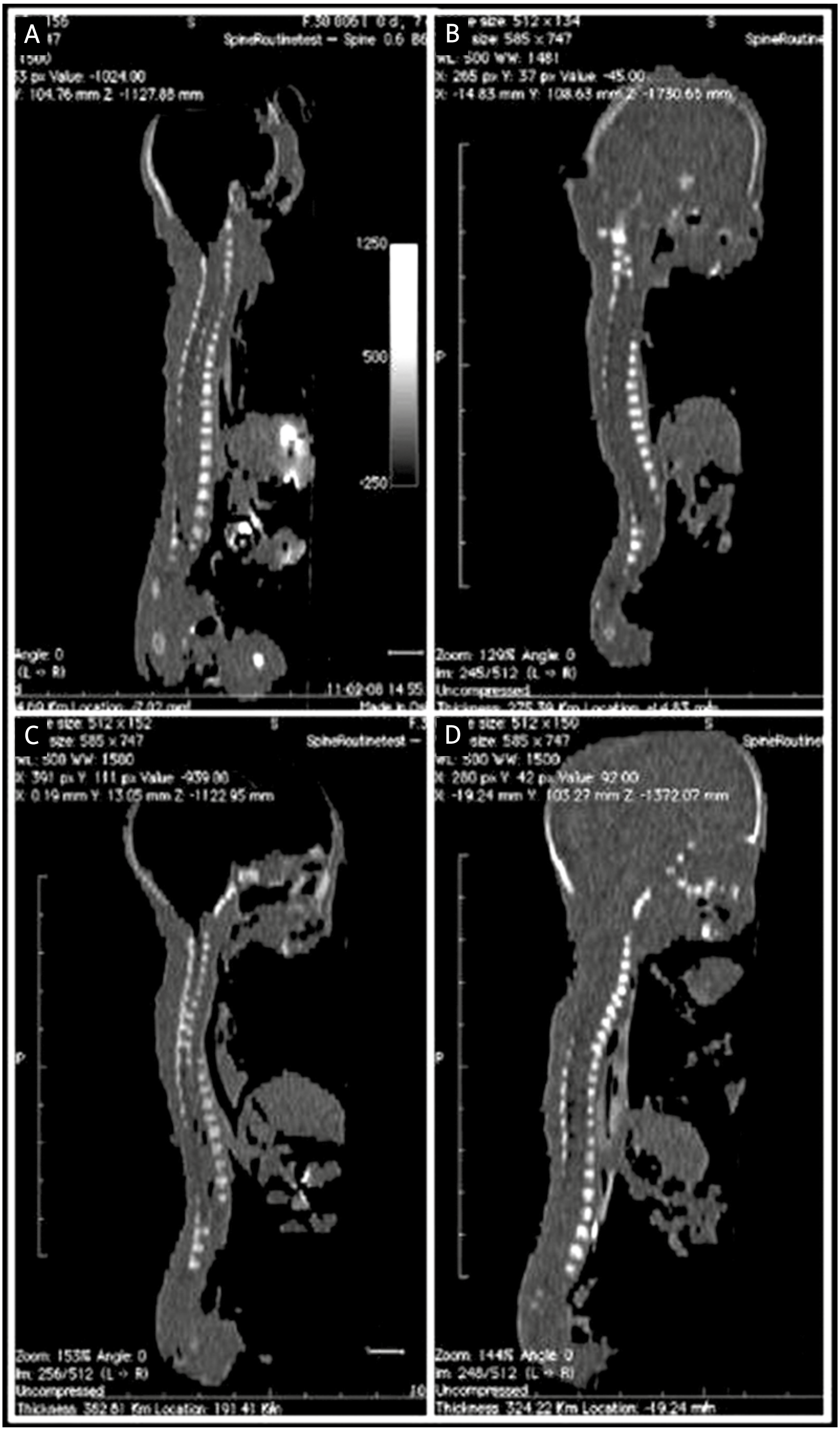

Figure 5. CT images of fetuses aged 25 (**A**), 26 (**B**), 27 (**C**), and 28 (**D**) weeks in the sagittal projection recorded in DICOM formats

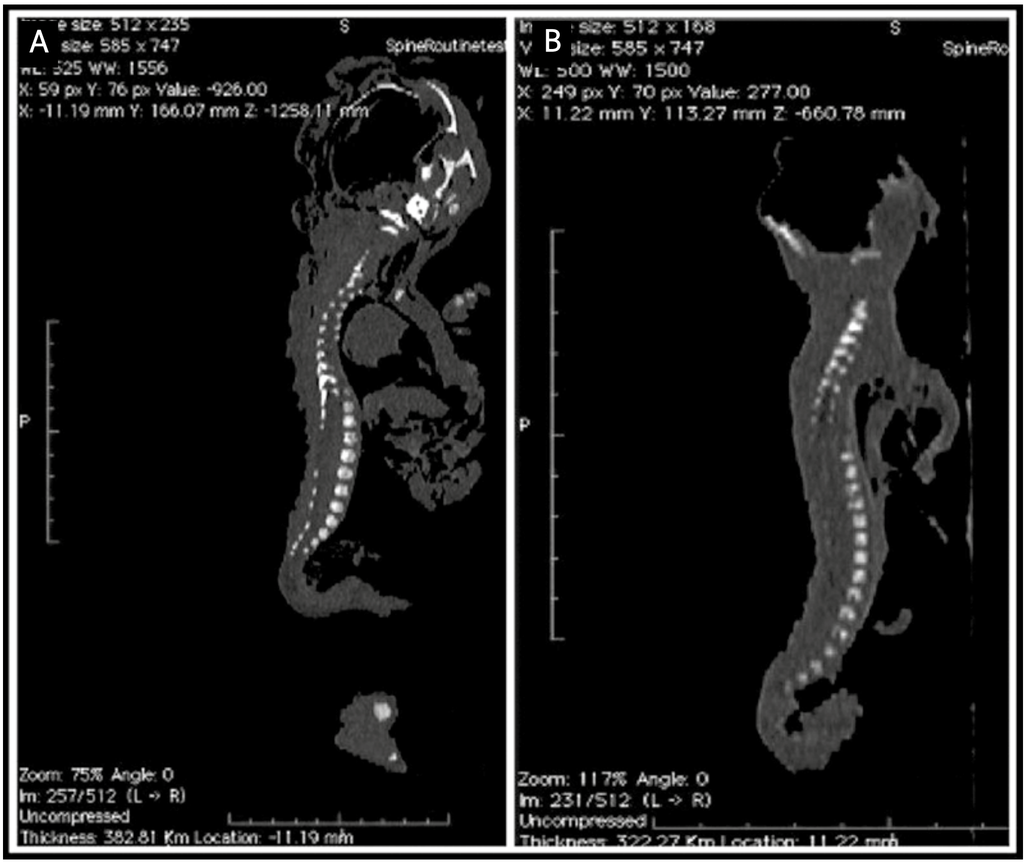

Figure 6. CT images of fetuses aged 29 (**A**), and 30 (**B**) weeks in the sagittal projection recorded in DICOM formats

L4 (113.67 ±75.29 mm^3), through vertebrae S1 (71.88 ±64.32 mm^3) and S3 (29.21 ±32.20 mm^3) to S5 (1.60 ±7.00 mm^3). The volumes of the T3 and S1 vertebral bodies, 71.12 ±33.54 mm^3 and 71.88 ±64.32 mm^3 respectively, were approximately equivalent to each other.

Discussion

In the professional literature the fetal spine used to be described as having exclusively the primary forwards concave curvature, reflecting the original shape of the embryo [19]. Therefore, the two secondary curvatures were to develop after birth, when a child was able to hold up its head and to sit upright (cervical lordosis), and later when a child started to stand and walk (lumbar lordosis). With the use of radiography, Bagnall *et al*. [20] paid particular attention to the development of the cervical lordosis in 195 human fetuses aged 8–23 weeks. Well-defined cervical lordosis was found in 83% of cases. In the remaining fetuses the cervical spine was either straight (11%) or even kyphotic (6%), as the continuation of the primary thoracic kyphosis. According to these authors, besides fetal respiratory movements, the early appearance of the cervical lordosis mostly resulted from fetal head extension as a basic component of the primitive "gasp" reflex. This explanation is firmly supported by early ossification in the occipital squama, which provides extensive anchorage for nuchal muscles [23]. As far as the lumbar lordosis is concerned, its constant (100%) presence in 45 fetuses aged 23–40 weeks was mathematically proved by Choufani *et al*. [2] on computerized MRI DICOM images. Of note, the lumbar lordosis showed no correlation with gestational age. The values of the lumbar lordosis varied from –0.133 to –0.033 mm^{-1} (minus for lordosis and plus would be for kyphosis), with the mean value of –0.054 mm^{-1}. In addition to that, the corresponding radius of the lumbar lordosis ranged from –7 to –303 mm with the mean value of –18.7 mm. It should be emphasized that in every fetus under examination, apart from the two primary thoracic and sacral kyphoses, we found the two secondary lordoses in keeping with Bagnall *et al*. [20] and Choufani *et al*. [2].

The present study attempts to extend the existing literature concerning the growth of vertebral bodies during fetal development in humans. The evidence material comprised 5 results for each vertebra and 145 results for each fetus, resulting in 7975 numerical data for the whole series. The values for vertebral bodies in the material under examination could be considered as both normative and real because of the following 5 reasons:

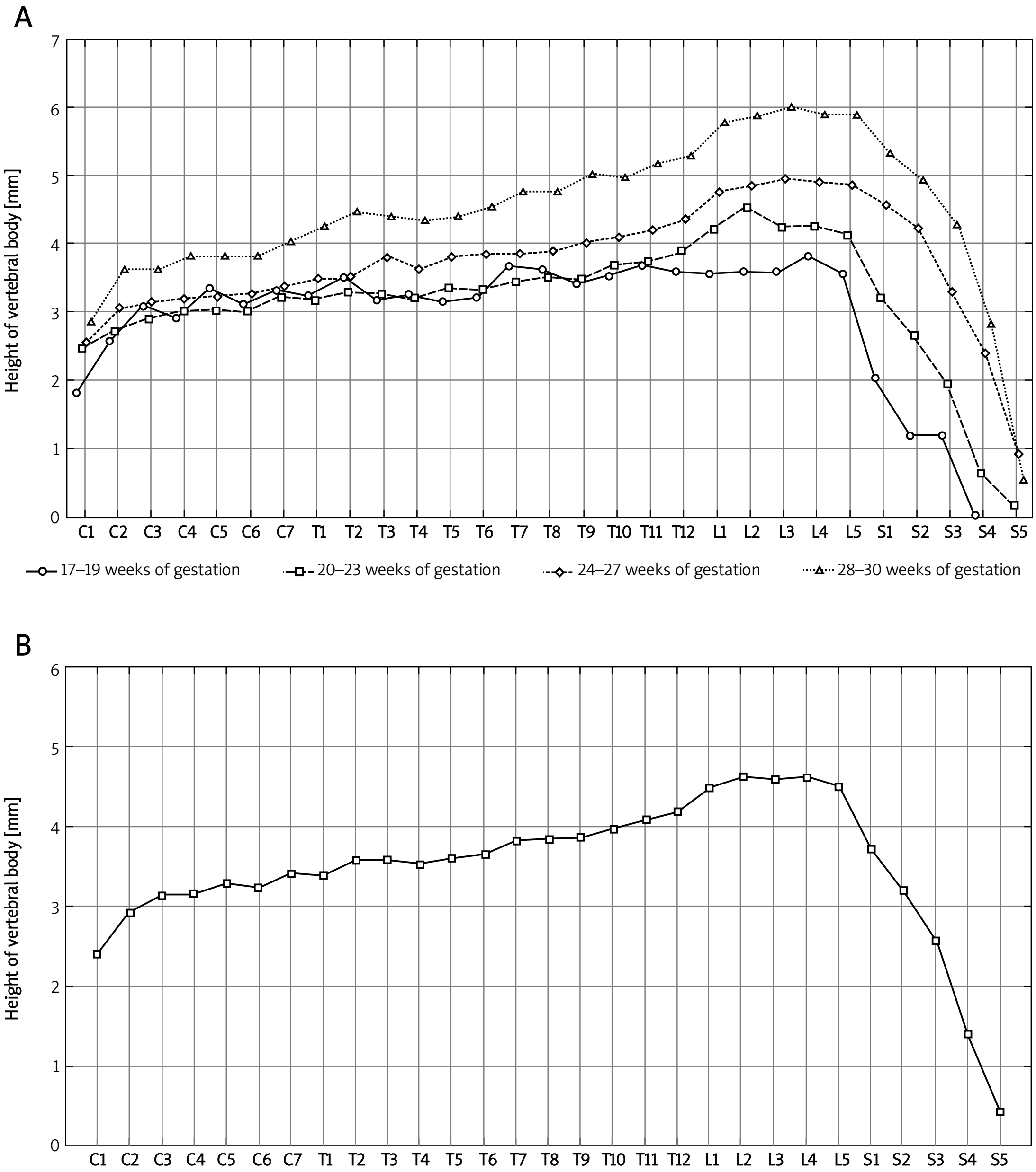

Figure 7. Mean height of individual vertebral bodies in fetuses aged 17–19, 20–23, 24–27, and 28–30 weeks of gestation (**A**), and for all the fetuses (**B**)

1) the fetuses constituted a numerous (n = 55) sample size with neither visible non-osseous nor osseous malformations,
2) tissue shrinkage related to formalin immersion had little influence on the values obtained [24–27],
3) valid objectives methods (Biograph mCT, Osirix 3.9) were used for evaluating all the parameters, with the greatest accuracy in measuring the selected dimensions to the nearest 0.01 mm,
4) the 4 parameters studied were precise and clearly definable, and
5) their calculation was based on direct measurements only, instead of deduced, extrapolated through a series of indirect measurements.

On the other hand, the main limitation of the present study resulted from a relatively narrow fetal age, varying from 17 to 30 weeks of gestation. Besides, all the measurements were done by one observer in a blind fashion. Finally, our findings have been presented as if describing a developmental sequence in one fetus, even though the numerical data are truly cross-sectional, derived from 55 autopsied fetuses.

Although significant sex differences resulting in a slightly more rapid rate of spinal ossification in female than in male fetuses have been reported in the medical literature [28], our results concerning the C1–S5 vertebral bodies did not support that

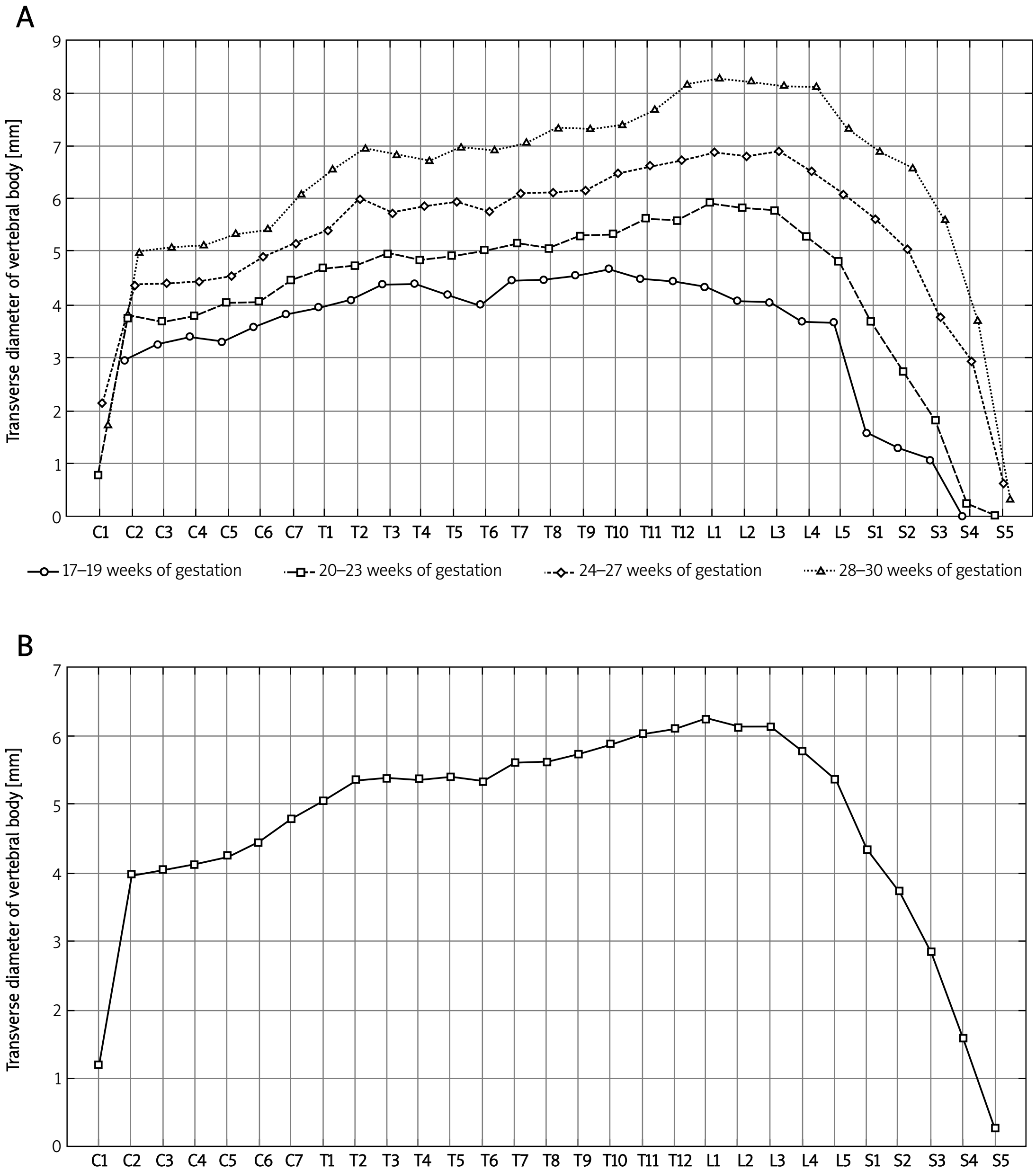

Figure 8. Mean transverse diameter of individual vertebral bodies in fetuses aged: 17–19, 20–23, 24–27, and 28–30 weeks of gestation (**A**), and for all the fetuses (**B**)

hypothesis. On the contrary, the numerical data of vertebral bodies obtained in our series were beyond the influence of sex, making us display them without regard to sex.

Since the vertebral body growth is three-dimensional, increases in transverse and sagittal diameters, cross-sectional area, and volume follow simultaneously with advancing gestational age. As exemplified in the present study, an understanding of spinal growth patterns can be achieved by studying all the C1–S5 vertebrae in every fetus. It is noteworthy that the shape of the curves representing the values for the 5 examined parameters was similar in any age range. Due to this, the mean values turned out to be representative of the whole series. There was a conspicuous increase in the body size between the atlas and the axis. This may result from the fact that the C1 vertebral body has no weight-bearing function, being fused onto the C2 vertebral body to become its dens. A gradual increase in all the values of vertebral bodies stood out from the axis to vertebra L2 for height (4.62 ±0.97 mm), to vertebra T7 for sagittal diameter (4.76 ±0.85 mm), to vertebra L1 for transverse diameter (6.24 ±1.46 mm), to vertebra L3 for cross-sectional area (24.92 ±11.07 mm^2), and finally to vertebra L3 for volume (122.16 ±74.73 mm^3). Thus, the L3 vertebral body was characterized by maximum

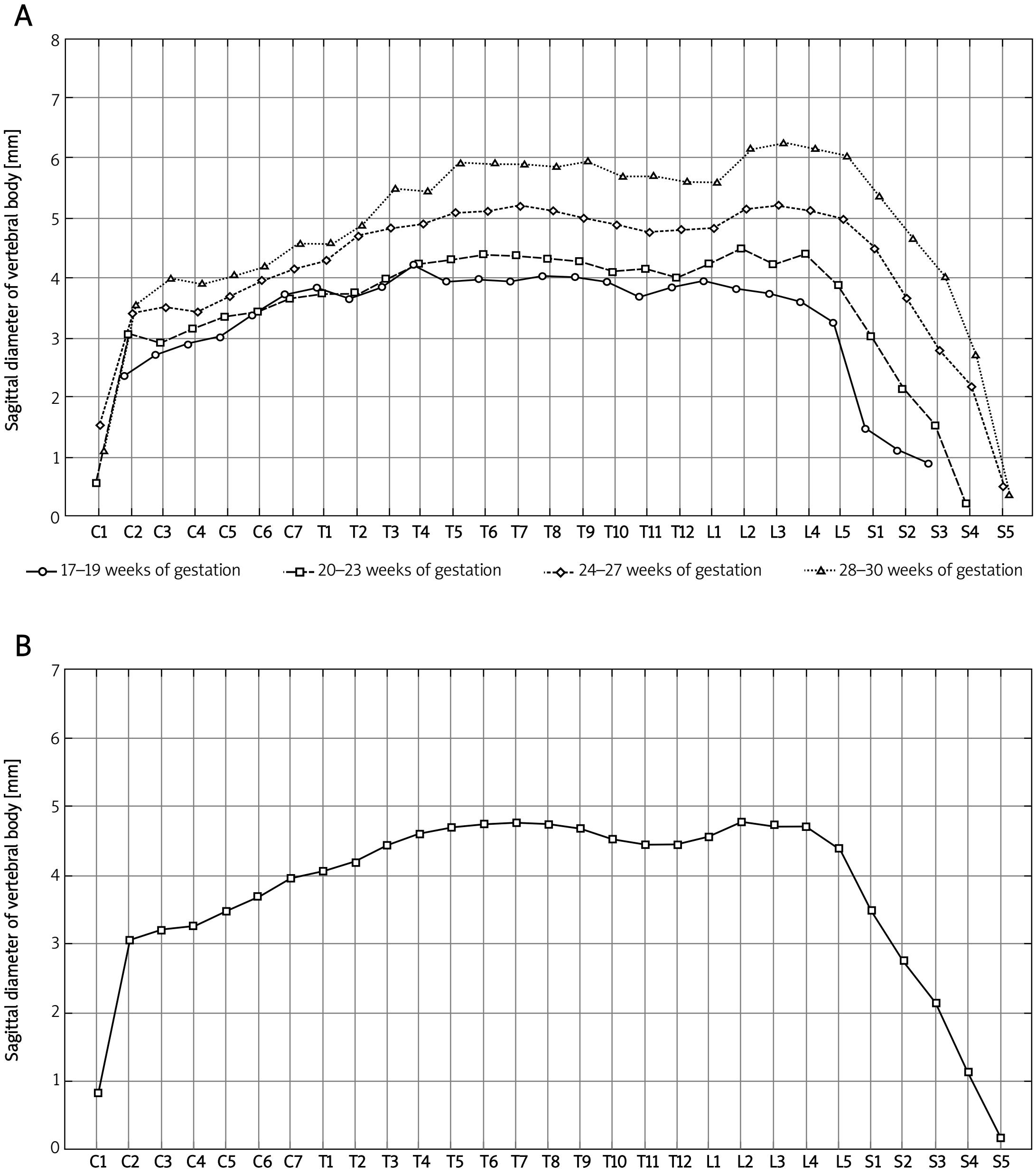

Figure 9. Mean sagittal diameter of individual vertebral bodies in fetuses aged 17–19, 20–23, 24–27, and 28–30 weeks of gestation (**A**), and for all the fetuses (**B**)

values for both cross-sectional area and volume. On the whole, the largest values of all the examined parameters were related to the lower thoracic-upper lumbar vertebrae. To best of our knowledge, this is a direct consequence of the timing of ossification, since vertebral bodies start to ossify with the inferior thoracic-superior lumbar segment [29–31], from which vertebral body ossification progresses both cranially and caudally. From a biophysical point of view, such a considerable increase in size of the inferior thoracic and superior lumbar vertebrae found in this study may be in part associated with the postnatal need to withstand greater stresses and strains. We found a phase of stabilized values at the levels of L3 (4.58 ±0.92 mm) – L4 (4.61 ±0.84 mm) for height, at the levels of L2 (6.12 ±1.65 mm) – L3 (6.12 ±1.61 mm) for transverse diameter, and at the levels of T8 (4.73 ±0.86 mm) – L4 (4.71 ±1.02 mm) for sagittal diameter. Finally, a sharp decrease in all the values of the sacral segment observed in the material under examination seems to be a consequence of the delayed appearance of sacral ossification centers [11].

The spine length has previously been reported to grow linearly [32–34], parabolically [21], or exponentially [1] with advancing gestational age. The thoracic spine length in human fetuses was expressed by the two following linear functions

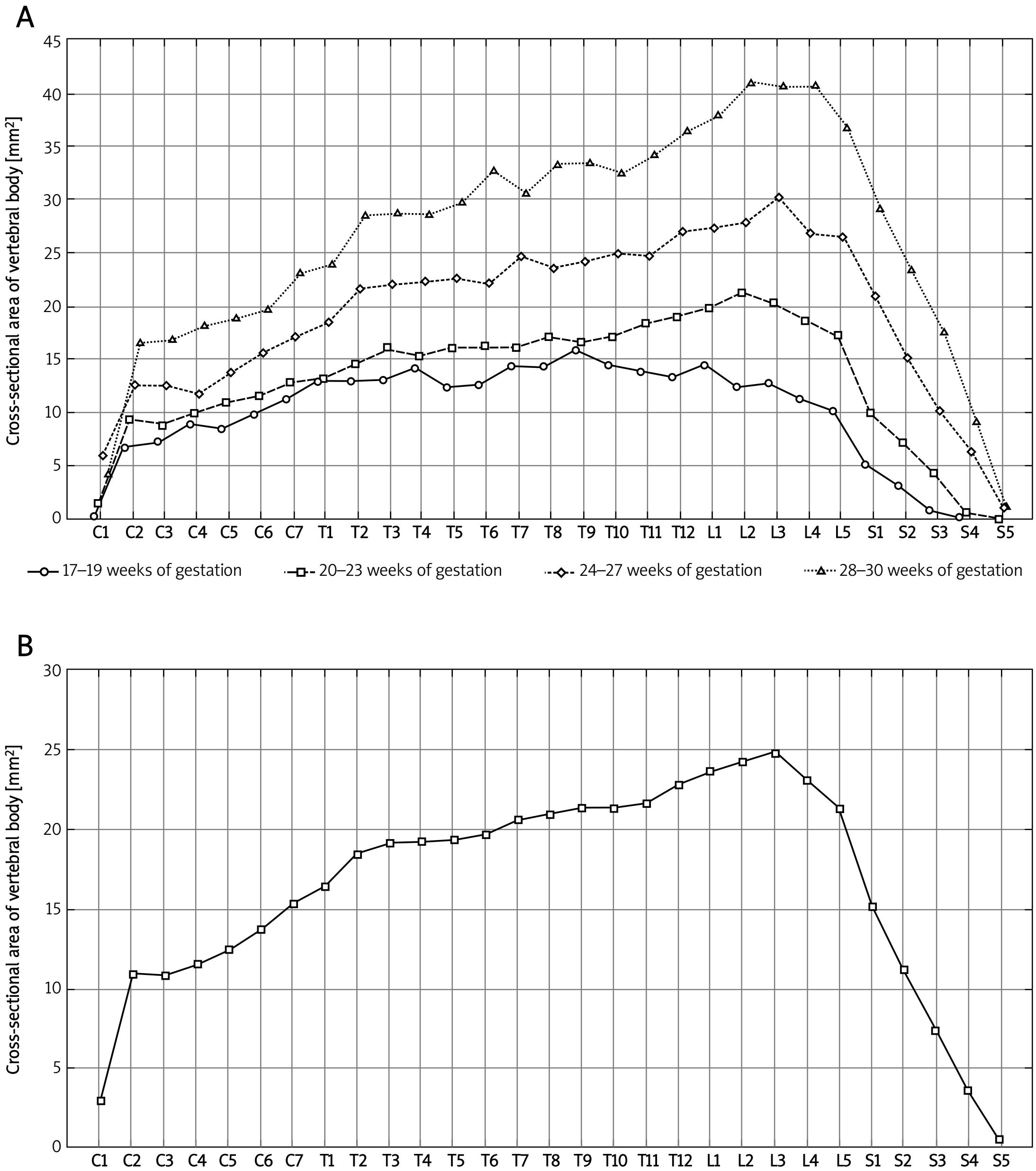

Figure 10. Mean cross-sectional area of individual vertebral bodies in fetuses aged 17–19, 20–23, 24–27, and 28–30 weeks of gestation (**A**), and for all the fetuses (**B**)

$y = 2.9 \times \text{age} - 17.8$ ($R^2 = 0.959$) [32] and $y = -10.85 + 1.627 \times \text{age}$ ($R^2 = 0.865$) [33]. As reported by Shin *et al*. [34], the height of vertebra L1 increased linearly from 3.8 ±0.3 mm in fetuses aged 26 weeks to 7.1 ±0.4 mm for the 41-week group of gestation. During that time the mean weekly increment in height of vertebra L1 was 0.23 mm in males and 0.20 mm in females. Bagnall *et al*. [21] showed that in fetuses aged 8–26 weeks, the spine length grew with age (in years) in a parabolic fashion, in the cervical part from 9 to 27 mm according to the function $y = -10.28 + 107.98 \times \text{age} - 67.35 \times \text{age}^2$ ($R = 0.90$), in the thoracic part from 25 to 60 mm in accordance with the function $y = -28.07 + 247.67 \times \text{age} - 691.97 \times \text{age}^2$ ($R = 0.99$), and in the lumbar part from 10.4 mm to 33.3 mm as the function $y = -16.11 + 133.83 \times \text{age} - 69.93 \times \text{age}^2$. Of note, the growth in length of each segment was characterized by a negative coefficient of the power 2, indicating a gradually decreasing rate of growth. Finally, the exponential function $y = \exp(4.705 - 32.4/\text{age})$ turned out to be the best model for the lumbar spine length [1].

Although the presacral spine was slowing down in its growth, both the cervical and lumbar parts still slowed to approximately half the growth rate of the thoracic segment [21]. As a result, in fetuses aged 8–26 weeks, the cervical part of the spine consti-

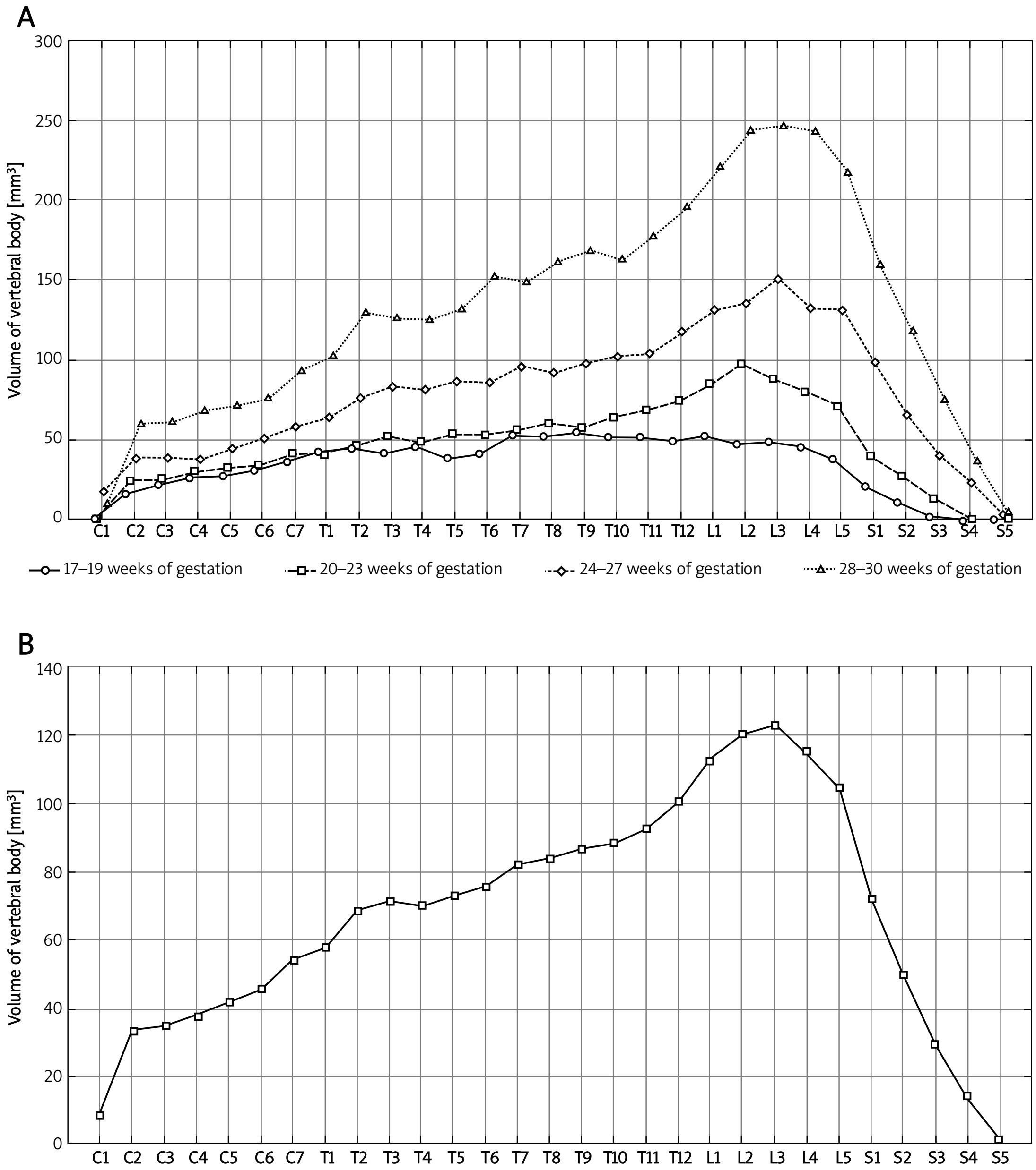

Figure 11. Mean volume of individual vertebral bodies in fetuses aged 17–19, 20–23, 24–27, and 28–30 weeks of gestation (**A**), and for all the fetuses (**B**)

tuted approximately 60% that of the thoracic one. In addition, the height of vertebra L1-to-body length ratio progressively increased with age, from 0.012 in fetuses aged 26–30 weeks to 0.014 in fetuses aged 36–41 weeks, with a considerable growth spurt in vertebra L1 at 34 weeks of gestation. For these reasons, the midpoint of the column shifted a little towards the cranium [35]. Furthermore, at 26 weeks of gestation the length of the "average" unit (vertebra plus disc) attained the value of 3.9 mm for cervical vertebrae, 5.0 mm for thoracic vertebrae, and 6.8 mm for lumbar vertebrae [21].

As reported by Tulsi [35], between 2–4 and 17–19 years the heights of vertebrae continued to increase by 39–45% for the cervical segment, by 36–47% for the thoracic part, and by 45–57% for the lumbar part. During that time the transverse and sagittal diameters of vertebral bodies increased by 6–12% and 20–33% for cervical vertebrae, 9–30% and 13–43% for thoracic vertebrae, and 44–53% and 39–48% for lumbar vertebrae, respectively.

The most accurate growth rate of vertebral bodies can be expressed by their volumetric analysis [1, 33]. Schild *et al.* [1] presented 3-dimensional ultrasound volume calculation of the T12, L1, L5 vertebral bodies, and the lumbar spine in fetuses aged 16–37 weeks. The growth in volume of vertebrae

Table II. Morphometric parameters of the C1–S5 vertebral bodies

Vertebra	Vertebral body									
	Height [mm]		Transverse diameter [mm]		Sagittal diameter [mm]		Cross-sectional area [mm²]		Volume [mm³]	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
C1	2.39	0.54	1.20	1.96	0.82	1.34	2.95	5.25	8.60	16.40
C2	2.92	0.46	3.98	0.86	3.07	0.60	10.88	4.33	33.12	17.68
C3	3.13	0.46	4.04	0.78	3.20	0.54	10.79	4.29	34.65	16.85
C4	3.16	0.46	4.12	0.74	3.26	0.46	11.36	3.40	36.20	15.85
C5	3.27	0.45	4.24	0.79	3.48	0.51	12.43	4.32	41.49	17.87
C6	3.23	0.41	4.43	0.82	3.68	0.48	13.65	4.42	45.36	19.82
C7	3.41	0.42	4.80	0.92	3.94	0.57	15.32	5.52	53.43	24.27
T1	3.38	0.63	5.04	0.98	4.04	0.52	16.40	5.27	58.15	26.38
T2	3.58	0.59	5.34	1.19	4.19	0.69	18.43	7.09	68.16	36.80
T3	3.58	0.60	5.37	0.98	4.44	0.75	19.12	6.21	71.12	33.54
T4	3.52	0.51	5.35	0.93	4.61	0.68	19.19	6.45	69.95	33.57
T5	3.60	0.55	5.40	1.07	4.70	0.83	19.32	7.07	72.64	37.42
T6	3.64	0.59	5.32	1.11	4.75	0.88	18.86	6.87	71.31	36.46
T7	3.81	0.60	5.60	1.03	4.76	0.85	20.58	7.39	81.90	42.63
T8	3.84	0.59	5.61	1.08	4.73	0.86	20.90	7.52	83.54	43.81
T9	3.86	0.64	5.72	1.05	4.68	0.81	21.31	7.64	86.35	46.21
T10	3.97	0.65	5.87	1.04	4.54	0.76	21.30	7.32	88.30	44.20
T11	4.08	0.66	6.01	1.22	4.46	0.78	21.62	7.80	92.17	47.93
T12	4.18	0.71	6.09	1.39	4.45	0.73	22.79	8.68	100.39	55.52
L1	4.47	0.86	6.24	1.46	4.55	0.63	23.62	8.68	112.30	61.60
L2	4.62	0.97	6.12	1.65	4.79	0.90	24.22	10.59	119.80	72.28
L3	4.58	0.92	6.12	1.61	4.72	0.98	24.92	11.07	122.16	74.73
L4	4.61	0.84	5.76	1.72	4.71	1.02	23.05	11.14	113.67	75.29
L5	4.50	0.93	5.36	1.48	4.40	1.12	21.32	11.04	104.43	71.34
S1	3.71	1.75	4.33	2.37	3.49	1.86	15.13	10.97	71.88	64.32
S2	3.18	1.91	3.75	2.44	2.77	1.74	11.18	9.05	49.56	47.44
S3	2.56	1.91	2.85	2.36	2.15	1.73	7.34	7.33	29.21	32.20
S4	1.39	1.80	1.58	2.23	1.16	1.64	3.59	5.86	13.78	24.70
S5	0.43	1.06	0.26	0.96	0.21	0.75	0.48	2.09	1.60	7.00

T12, L1, L5 and L1–5 ranged from 0.047 ml to 2.311 ml, 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: $y = \exp(2.79 - 86.94/\text{age})$ for vertebra T12 ($R^2 = 0.92$), $y = \exp(2.99 - 89.76/\text{age})$ for vertebra L1 ($R^2 = 0.92$), $y = \exp(2.74 - 90.81/\text{age})$ for vertebra L5 ($R^2 = 0.90$), and $y = \exp(4.94 - 89.81/\text{age})$ for vertebrae L1–5 ($R^2 = 0.94$). Between 2–4 and 17–19 years the volumetric growth of cervical, thoracic and lumbar vertebral bodies by 58–68%, 72–77%, and 75–88% respectively was reported, but with no regression models [35].

The present study is the first in the medical literature to provide objective information on the quantitative growth of the C1–S5 vertebral bodies in human fetuses. Our findings undoubtedly support the presence of two kyphoses and two lordoses in every fetal spine. Both the present CT images (Figures 1, 3–6) and normograms (Figures 7–11) display dimensions of the vertebral bodies and improve our knowledge of spinal quantitative morphology in formalin-fixed human fetuses. All the parameters presented in this study may serve as a useful reference to anatomists dealing with developmental growth patterns in the fetus. Of note, since formalin immersion exerts little influence on the spine [24–26], the results obtained in the material under examination can directly be adapted *in vivo* to the fetal and neonatal spine. The prenatal ultrasound diagnosis or exclusion of spinal defects is based on an understanding of normal primary spinal ossification [11, 29–31, 36]. Our quantitative data as relevant fetal age-specific references for vertebral bodies throughout the spine may considerably help to recognize in fetuses the following malformations: caudal regression syndrome, hemivertebra, butterfly vertebra, achondrogenesis, and osteogenesis imperfecta type II. Caudal regression syndrome as a spinal defect ranges from isolated sacral agenesis to complete lumbar-sacral agenesis [11, 37–39]. Hemivertebra results from unilateral agenesis of one of the two chondrification centers within a vertebral body. This results in a defective triangular wedge-shaped vertebral body [12–16]. On the other hand, in butterfly vertebra two chondrification centers failed to fuse, being separated from each other by the persistent notochord [17, 40]. As a result, both hemivertebra and butterfly vertebra are characterized by significantly reduced dimensions, including their height, transverse and sagittal diameters, cross-sectional area, and volume. Since the sacral bodies normally ossify before the sacral arches, delayed sacral body ossification when compared to the sacral arches is typical of achondrogenesis [10, 11]. Osteogenesis imperfecta type II [41, 42], achondrogenesis [10], hypophosphatasia [18], and phenylketonuria [43] are characterized by delayed appearance of ossification centers and widespread demineralization. As a consequence, the 5 aforementioned diseases contribute to smaller dimensions of vertebral bodies [10, 18, 41, 43].

In conclusion, every fetal spine was characterized by two kyphoses and two lordoses. The vertebral body dimensions do not reveal sex differences. There is a sharp increase in size of fetal vertebral bodies between the atlas and the axis, and a sharp decrease in size within the sacral spine. In human fetuses the vertebral body growth is characterized by the maximum sagittal diameter for T7, the maximum transverse diameter for L1, the maximum height for L2, and the maximum both cross-sectional area and volume for L3.

Conflict of interest

The authors declare no conflict of interest.

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