Morphometric (MRI and sonography) study of the human spinal cord in prenatal and postnatal life (from birth to 20 years)

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Introduction
The assessment of the position of the conus medullaris is very important to perform lumbar puncture and surgical procedures. There are some reports about the relationships between the clinical manifestations and the spine morphology or spinal cord morphology in patients with myelopathy. It has also been reported that there are variations in the cross-sectional area of the cervical segments of the spinal cord.

Aim
The aim of the present study was to compare the levels of conus to measure the diameters of the cervical spinal cord segments.

Participants and methods
In the prenatal group, sonographic evaluation of the conus medullaris and the conus distance were carried out. In the postnatal group, the T2-weighted MRI was used to record the level of conus medullaris. In addition, the transverse and anteroposterior diameter of the cervical spinal cord and cross-sectional area from C2 to T1 at the level of each intervertebral disk were investigated.

Results
In the prenatal group, the mean of conus distance was 32.38 ± 12.13 mm. The level of the tip of the conus medullaris in the postnatal group showed almost distribution from the T12 to L2–L3 disk. The peak of the distribution of the conus height was at the level of disk between T12 and L1. The anteroposterior diameter decreased linearly from C2 to T1.The transverse diameter and the cross-sectional area were largest at the level of C4–C5, and decreased progressively to segment T1. There was no statistically significant difference in relation to sex.

Conclusion
Linear regression analysis showed a significant correlation between the conus distance and gestational age and femur length. The ascent of conus medullaris seems to occur early in postnatal life. The transverse diameter and the cross-sectional area were largest at the level of C4–C5, whereas the anteroposterior diameter decreased from C2 to T1.There was no significant correlation between cervical diameters and sex.

Keywords:
cervical segment, conus distance, conus medullaris, MRI

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Introduction

The ascent of the conus medullaris with respect to the adjacent vertebral column during fetal and postnatal development and its ultimate level of termination postnatally have been the subject of several studies using both cadavers and various imaging modalities.

Knowledge of the embryologic development and normal anatomy of the spinal cord and their variants are prerequisites for diagnosis of congenital and acquired diseases of this structure. Exclusion of spinal defects such as open spina bifida is one of the main objectives in fetal anomaly scanning [1].

It is widely known that MRI is an extremely accurate and practical way to evaluate the spinal cord and a more accurate method of determining the location of the conus medullaris terminus compared with cadaveric examination [2].

One of the major concerns during needle insertion for spinal anesthesia is the location of the conus medullaris terminus. Anesthesiologists remain aware that any maneuver that places the spinal needle in contact with the spinal cord may lead to serious neurological injury [3].

In the treatment of cervical spinal disorders, such as compressive myelopathy and spinal cord injury,

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the transverse area of the cervical spinal cord of the patient has been considered as an effective predictor of clinical outcomes. Several authors have reported that the decreased spinal cord area before decompressive surgery would indicate poor surgical outcomes [4]. Morphometric studies of the normal human spinal cord have been performed using computed tomographic myelography [5] and MRI [6].

This study aimed to compare the levels of conus medullaris in prenatal life and postnatal life in young ages to show the time of ascent to normal. In addition, the study aimed to measure the diameters of the cervical spinal cord segments of healthy people and to evaluate the relationships between these diameters and sex.

Participants and methods

This study was conducted on 60 pregnant women and 120 normal persons. They were divided into two groups. Ethical Committee of Benha University approved this research.

First prenatal group comprised 60 pregnant women who visited Benha University Hospital for follow-up and underwent ultrasound examination, representing the gestational age (GA) from fourth month till ninth month of pregnancy. This study involved three-dimensional (3D) ultrasound examinations.

A Voluson-730Prov ultrasound system with a transabdominal 3D volume probe (5–8 MHz) was used in the present study. The following settings were put in place when acquiring these 3D volume data sets: power, 100%; gain, 0.0; tissue harmonic imaging, on (low); angle (view), 70°; angle (sweep), 65°; and sweep speed, 4–10 s. All images remained stored on the machine's internal hard drive for further image analyses. The images showed the conus medullaris and the last ossification center of the vertebral body. In addition, the distance between the most caudal point of the conus medullaris and the last ossification of the sacrum (conus distance) was measured. The femur length (FL) was also measured.

Second postnatal group comprised 120 normal volunteers who attended Ain Shams outpatient clinic, Egypt, for whole-spine MRI. They were subdivided into three subgroups. Each subgroup comprised 20 males and 20 females. The age of the first subgroup ranged from first year up to less than 7 years. The age of second subgroup ranged from seventh year up to less than 12th year. The age of the first subgroup ranged from first year up to less than 7 years. The age of the second subgroup ranged from seventh year up to less than 12th year. The age of the third subgroup ranged from 12 to 20 years.

MRI scans were performed with a 1.5-T superconductive magnet (Signa Horizon Excite HD version 12; GE Healthcare). Scans were taken at slice thicknesses of 3 and 4 mm in the sagittal and axial planes, respectively. In sagittal scans, T1-weighted images [fast spin-echo repetition time (TR), 450 ms; echo time (TE), 8.1 ms] and T2-weighted images (fast spin-echo TR, 3500 ms; TE, 102 ms) were obtained. Axial scans were performed using T2-weighted images (fast spin-echo TR, 4000 ms; TE, 102 ms). All images were transferred to the computer as DICOM data.

Through the sagittal view of whole spine MRI, the length of spinal cord was obtained. The termination of the conus medullaris was identified relative to the adjacent vertebrae, with each vertebral body divided into upper, middle, and lower third, and the intervertebral disk space serving as a fourth level. Through the axial view, the slices taken at cervical vertebrae were made at the intervertebral levels from the second cervical to first thoracic vertebrae, and the anteroposterior and transverse diameters crossing central canal of the spinal cord and cross-sectional area for each level were measured.

The height of the person and the upper-segment length were calculated.

Results

The recorded parameters in first group (prenatal life)

Three-dimensional ultrasound was carried out on 60 fetuses of pregnant women from fourth month of GA till term. The mean of GA at the time of ultrasonography examination was 27.47 ± 6.41 weeks (range = 18–38 weeks). Mean of FL was 51.19 ± 32.38 mm (range = 28.5–78.1 mm). Mean conus distance was 32.38 ± 12.13 mm (range = 7.6–51.1 mm) (Table 1 and Fig. 1).

Linear regression analysis showed a highly significant association between the conus distance and GA ($R^2 = 0.8876$, $P < 0.001$), and the best-fit formula for this correlation was conus distance=1.7831 × GA–16.594 (Histogram 1). Another linear regression analysis

Table 1 Range and mean of gestational age, femur length, and conus distance

Parameters	Studied group	
	Range	Mean ± SD
Gestational age	18–38 weeks	27.47 ± 6.41 weeks
Femur length	28.5–78.1 mm	51.19 ± 32.38 mm
Conus distance	7.6–51.1 mm	32.38 ± 12.13 mm

showed a highly significant association between the conus distance and FL (R^2 = 0.8526, P < 0.001), and the best-fit formula for this correlation was conus distance = 0.8162 × FL-9.4004 (Histogram 2).

The recorded parameters in second group (postnatal life)

Whole-spine MRI was carried out on the vertebral column of 120 volunteers including 60 females (F) and 60 males (M), with an age range of 1–20 years. The level of the tip of the conus medullaris showed almost distribution from the T12 to the disk between L2 and L3. The peak of the distribution of the conus height was at the level of disk between T12 and L1.

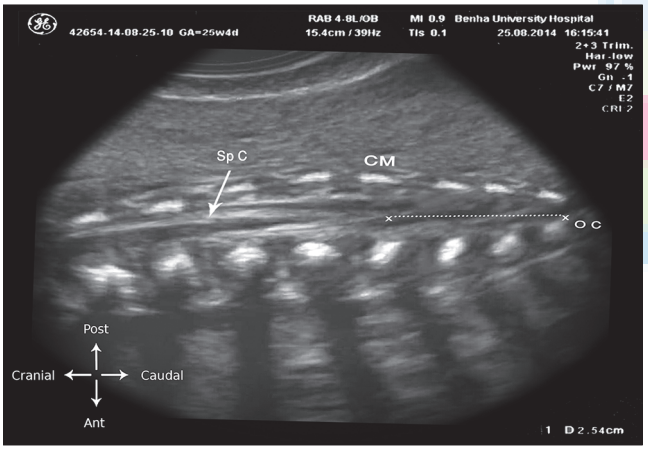
Through the comparison between the three aged subgroups, the level of the tip of the conus medullaris showed 27.5% at the intervertebral disk between T12 and L1 and 27.5% at the lower level of L1 in the first subgroup, 30% at the intervertebral disk between T12 and L1 in the second subgroup, and 35% at the intervertebral disk between T12 and L1 in the third subgroup. The comparison of the conus level had no significant relationship to age (Table 2).

Through the comparison between male and female volunteers, the level of the tip of the conus medullaris showed almost distribution at the level of disk between T12 and L1, 28.3% in male and 33.3% in female. The comparison of the conus level had no significant relationships to sex (Table 3).

The mean height of volunteers was 89.67 ± 14.67 cm in the first age group, 121.5 ± 6.3 cm in the second age group, and 162.75 ± 9.01 cm in the third age group, whereas the mean of upper-segment length was 379.35 ± 72.13, 559.32 ± 50.78, and 679.18 ± 46.95 mm, respectively. The mean length of spinal cord was 222.15 ± 31.32 mm in the first age group, 256.68 ± 27.01 mm in the second age group, and 322.42 ± 49.92 mm in the third age group. The mean of the ratio of the length of spinal cord to the age, upper-segment length, and the height of volunteer in the first age group, the second age group, and the third age group showed high statistically significant change (Fig. 2).

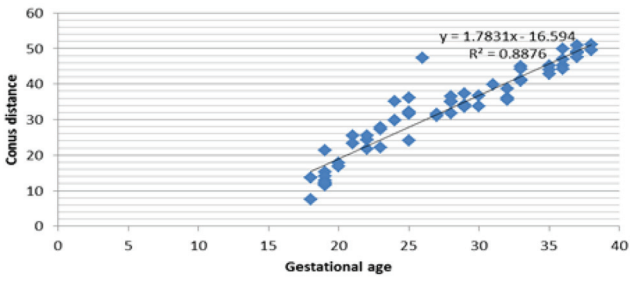
On the other hand, the 40 volunteers underwent MRI of the cervical spine. The group included 20 males and 20 female, aged 12–20 years.

Figure 1



Ultrasonography of the fetal spine aged 25th week of gestational period shows the spinal cord (SpC) and its conus medullaris (CM) in relation to ossific centers (OC) of the vertebral column. Note that the dotted line extends between CM and last OC (2.54 cm).

Histogram 1



It shows linear correlation between conus distance and gestational age.

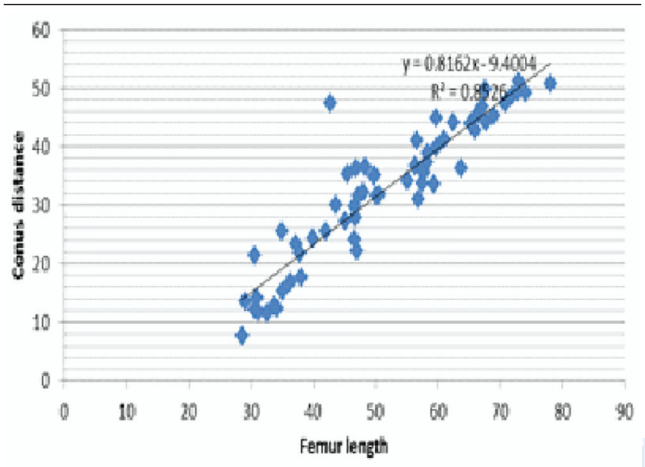
Table 2 Comparison between the three aged subgroups according to level of conus medullaris in whole-spine MRI

	Age groups					
Level of conus medullaris	Group I [*n* (%)]	Group II [*n* (%)]	Group III [*n* (%)]	Total [*n* (%)]	FET	*P* value
T12 lower level	2 (5.0)	0 (0.0)	0 (0.0)	2 (1.7)		
T12–L1	11 (27.5)	12 (30.0)	14 (35.0)	37 (30.8)	26.12	0.052
L1 middle level	10 (25.0)	10 (25.0)	11 (27.5)	31 (25.8)		NS
L1 lower level	11 (27.5)	7 (17.5)	10 (25.0)	28 (23.3)		
L1–L2	4 (10.0)	4 (10.0)	0 (0.0)	8 (6.7)		
L2 upper level	0 (0.0)	2 (5.0)	0 (0.0)	2 (1.7)		
L2 middle level	0 (0.0)	0 (0.0)	2 (5.0)	2 (1.7)		
L2 lower level	0 (0.0)	5 (12.5)	3 (7.5)	8 (6.7)		
L2–L3	2 (5.0)	0 (0.0)	0 (0.0)	2 (1.7)		
Total	40 (100)	40 (100)	40 (100)	120 (100)		

FET, Fisher exact test.

It can be seen that the anteroposterior diameter decreased linearly from C2 to T1 (Table 4), became a line at the level of C5–C6 and C6–C7 intervertebral disks and then continued to decrease. The transverse diameter and cross-sectional area were at their largest at the level of C4–C5, and decreased progressively to segment (Tables 5 and 6). It increased from the level C2–C3 to the main peak at segment C5 and then decreased markedly toward the upper thoracic segments. No statistically significant difference in the cervical segment diameters was recorded between male and female (Fig. 3).

Histogram 2



It shows linear correlation between conus distance and femur length.

Discussion

The anatomy of the spinal cord is well established from histology, but remains somewhat obscured by present-day clinical radiological standards. In animal studies, the cord anatomy has been properly visualized, but the spatial detail achievable in the clinical setting is much more limited, thus limiting the radiologist's ability to identify small-scale lesions or structures that may relate to neurological deficits, as well as limiting the accuracy of neurodegenerative atrophy measurements [7]. Recently, it has become evident that MRI is the best clinical tool for evaluating traumatic spinal cord injury, and is therefore invaluable for not only the degree of spinal canal stenosis but also the detailed intramedullary status of the spinal cord [8].

Prenatal evaluation of the conus medullaris

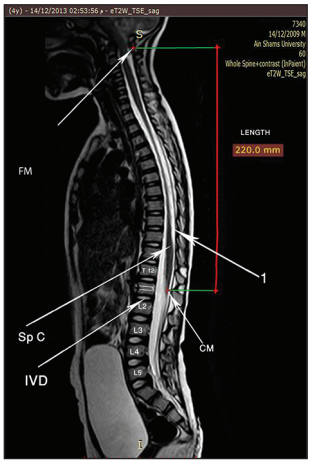
There was a significant correlation between GA and distance of conus medullaris, and also a significant

Table 3 The comparison between male and female of the postnatal group in relation to level of conus medullaris in whole-spine MRI

	Sex				
Level of conus medullaris	Male [*n* (%)]	Female [*n* (%)]	Total [*n* (%)]	FET	*P* value
T12 lower level	0 (0.0)	2 (3.3)	2 (1.7)		0.288 (NS)
T12–L1	17 (28.3)	20 (33.3)	37 (30.8)		
L1 middle level	16 (26.7)	15 (25)	31 (25.8)	9.09	
L1 lower level	11 (18.3)	17 (28.3)	28 (23.3)		
L1–L2	6 (10.0)	2 (3.3)	8 (6.7)		
L2 upper level	2 (3.3)	0 (0.0)	2 (1.7)		
L2 middle level	1 (1.7)	1 (1.7)	2 (1.7)		
L2 lower level	5 (8.3)	3 (5.0)	8 (6.7)		
L2–L3	2 (3.3)	0 (0.0)	2 (1.7)		
Total	60 (100)	60 (100)	120 (100)		

FET, Fisher exact test; $P > 0.05$, insignificant (NS).

Figure 2



MRI in midsagittal plane of the whole spine of male person aged 4 years shows the length of the spinal cord (SpC) from foramen magnum (FM) to the conus medullaris (CM) is measured 220 mm. The CM lies at the middle level of L1. Note (1) represents subarachnoid space. L5, L4, L3, L2, L1, T12 and intervertebral disk (IVD).

Table 4 The anteroposterior diameter of the cervical segment of spinal cord in relation to male and female

Anteroposterior	Male		Female		Student *t*-test	*P* value
	Range (mm)	Mean ± SD (mm)	Range (mm)	Mean ± SD (mm)		
C2–C3	4.5–7.1	5.39 ± 0.96	4.5–6.5	5.28 ± 0.64	0.407	0.686 (NS)
C3–C4	3.9–6.9	5.23 ± 0.64	3.9–5.8	4.92 ± 0.697	1.28	0.209 (NS)
C4–C5	3.9–5.7	4.57 ± 0.71	3.6–5.7	4.5 ± 0.51	0.359	0.721 (NS)
C5–C6	4–6.4	4.97 ± 0.79	3.9–5.9	4.66 ± 0.65	1.36	0.183 (NS)
C6–C7	3.6–6.3	5.1 ± 0.94	3.6–6.4	4.61 ± 0.87	1.69	0.099 (NS)
C7–T1	3.4–6.4	4.64 ± 0.86	3.7–5.1	4.33 ± 0.502	1.40	0.171 (NS)

Table 5 The transverse diameter (T) of the cervical segment of spinal cord in relation to male and female

Transverse diameter	Male		Female		Student *t*-test	*P* value
	Range (mm)	Mean ± SD (mm)	Range (mm)	Mean ± SD (mm)		
C2–C3	9.2–11.7	10.06 ± 0.79	8.1–12.3	10.36 ± 1.35	0.856	0.397 (NS)
C3–C4	10.1–13.5	11.47 ± 0.96	9.5–13.4	11.19 ± 1.2	0.814	0.42 (NS)
C4–C5	9.9–14.1	11.85 ± 1.34	9.9–14.7	11.67 ± 1.54	0.395	0.695 (NS)
C5–C6	8.5–13.3	11.17 ± 1.4	9–14.1	11.3 ± 1.43	0.291	0.773 (NS)
C6–C7	8.3–12.9	10.37 ± 1.48	8.3–12.9	10.54 ± 1.51	0.349	0.729 (NS)
C7–T1	7–11.3	8.66 ± 1.39	7–9.8	8.63 ± 1.01	0.078	0.938 (NS)

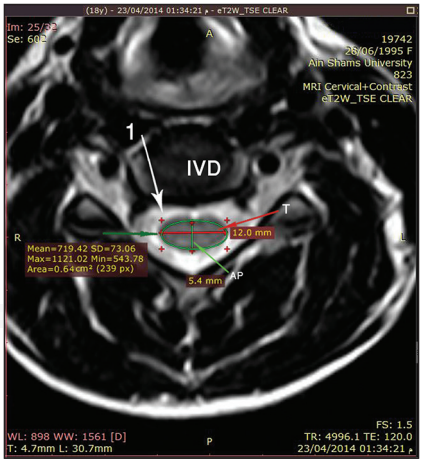
Table 6 The cross-sectional area of the cervical segment of spinal cord in relation to male and female

Cross-sectional area	Male		Female		Student *t*-test	*P* value
	Range (mm^2)	Mean ± SD (mm^2)	Range (mm^2)	Mean ± SD (mm^2)		
C2–C3	60–100	80.91 ± 10.98	66.25–90	78.92 ± 7.57	0.667	0.509 (NS)
C3–C4	70.25–100.20	87.43 ± 7.69	70.25–93	85.8 ± 6.62	0.718	0.477 (NS)
C4–C5	75.5–101	91.25 ± 8.27	79.5–101	92.83 ± 7.88	0.617	0.541 (NS)
C5–C6	66.75–101.5	88.68 ± 11.36	70.5–100	87.63 ± 9.25	0.318	0.752 (NS)
C6–C7	59–98	80.36 ± 12.39	59–91	79.4 ± 9.87	0.272	0.787 (NS)
C7–T1	57–88.25	70.91 ± 10.11	56–79	69.43 ± 8.4	0.506	0.616 (NS)

correlation between FL and conus distance. This obtained result was in agreement with studies conducted by Hoopman *et al.* (2011) [9] and Rodriguez *et al.* (2014) [10], which found a linear relationship between conus distance and GA and a stronger relationship between conus distance and FL.

Through this study, the regression formula was easy to use, as the expected conus distance can be calculated as follows: conus distance = 0.82 × FL-9.4. The formula for the relation between conus distance and GA is as follows: conus distance = 1.78 × GA–16.6. The regression equation between conus distance and FL, put forward by Hoopman *et al.* (2011) [9], is as follows: conus distance = –8.2 + FL, whereas the equation put forward by Rodriguez *et al.* (2014) [10] for the relation between conus distance and FL conus distance was 1.03 × FL-6.70, and for the relation between conus distance and GA was conus distance was 2.34 × GA–19.15.

Figure 3



T2-weighted MRI using axial view of 18 year old female shows anteroposterior diameter (AP), transverse diameter (T), and cross-sectional area of cervical segment of spinal cord at the level of intervertebral disk (IVD) of C4–C5. Note (1) represents subarachnoid space

Postnatal evaluation of the conus medullaris

This study revealed the location of conus medullaris to be close to the regular distribution of the conus in the others studies. Malas *et al.* (2000) [11], Arai *et al.* (2001) [12], Demiryürek *et al.* (2002) [13], Tame and Burstal (2003) [14], Lee *et al.* (2004) [15], Soleiman *et al.* (2005) [16], Kesler *et al.* (2007) [17], Sun *et al.* (2008) [18], Rahmani *et al.* (2011) [19], Moussallem *et al.* (2014) [20], and Van Schoor *et al.* (2015) [21] have examined the level of the conus medullaris in infants, children, and young adults using MRI. The range varied between the disk between T11 and T12 and the upper level of L3. The wide range may be due to use only lumbar spine images and counted up from the sacrum; neither the number of cervical vertebrae nor the number of rib-bearing vertebrae was assessed, and this may be due to racial difference.

There was no significant difference in conus medullaris level in relation to age, which is in agreement with several studies, including Saifuddin and colleagues (1998), Arai *et al.* (2001) [12], Demiryürek *et al.* (2002) [13], Moussallem *et al.* (2014) [20], and Van Schoor *et al.* (2015) [21].

No statistical difference was seen between male and female in all cases, and this is in agreement with the findings of Moussallem *et al.* (2014) [20], Arai

et al. (2001) [12], and Saifuddin *et al.* (1998) [22] who had also studied the conus position with MRI. However, results of this study do not support the studies by Lao *et al.* (2013) [23] and Demiryürek *et al.* (2002) [13].

The data obtained from cervical segments, showing no statistically significant changes for both sexes, were similar to the results of studies conducted by Lao *et al.* (2013) [23], Fradet *et al.* (2014) [6] and Kato *et al.* (2012) [24], which revealed, using 1.5-T MRI, that the anteroposterior diameter of the spinal cord at the C2/C3 intervertebral disk level was 6.9 ± 0.7 mm for males and 6.7 ± 0.7 mm for females, and it decreased gradually to 5.7 ± 0.6 mm in males and 5.5 ± 0.6 mm in females at the C7/T1, and the mean cross-sectional areas at C4 in males and females were 91.8 + 9.7 and 95.2 + 8.0 mm^2, respectively. This difference in numbers may be due to the use of more than 200 volunteers in the previous studies.

Conclusion

Conus distance is significantly correlated with both FL and GA. The conus medullaris terminates most commonly at the T12–L1 disk space, and in the absence of tethering the conus medullaris virtually never ends below the lower-body of L2 in persons aged 1–20 years.

The transverse diameter and the cross-sectional area were largest at the level of C4–C5 and decreased to segment T1while the anteroposterior diameter decreased from C2 to T1. There was no significant correlation between anteroposterior, transverse diameters, and cross-sectional area of the cervical segments and sex.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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