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Journal
The Journal of Pediatrics, 167(2)

ISSN
0022-3476

Authors
Ponrartana, Skorn
Aggabao, Patricia C
Dharmavaram, Naga L
et al.

Publication Date
2015-08-01

DOI
10.1016/j.jpeds.2015.04.078

Peer reviewed

HHS Public Access

Author manuscript

J Pediatr. Author manuscript; available in PMC 2016 August 01.

Published in final edited form as:

J Pediatr. 2015 August ; 167(2): 416–421. doi:10.1016/j.jpeds.2015.04.078.

Sexual Dimorphism in Newborn Vertebrae and its Potential Implications

Skorn Ponrartana, MD, MPH[1], **Patricia C. Aggabao, BA**[1], **Naga L. Dharmavaram, BS**[1], **Carissa L. Fisher, BS**[1], **Philippe Friedlich, MD, MS Epi, MBA**[2], **Sherin U. Devaskar, MD**[3], and **Vicente Gilsanz, MD, PhD**[1,2,*]

[1]Department of Radiology, Children's Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, CA

[2]Department of Pediatrics, Children's Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, CA

[3]Department of Pediatrics, Mattel Children's Hospital, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA

Abstract

Objective—To examine whether the sex-related differences in vertebral cross-sectional area (CSA) found in children and at the timing of peak bone mass – a major determinant of osteoporosis and future fracture risk – are also present at birth.

Study design—Vertebral CSA, vertebral height, and intervertebral disc height were measured using magnetic resonance imaging (MRI) in 70 healthy full-term newborns (35 male and 35 female). Additionally, measures of the length and CSA of the humerus, musculature, and adiposity were obtained.

Results—Weight, body length, and head and waist circumferences did not significantly differ between sexes (all P's ≥ 0.06). Compared with newborn boys, girls had significantly smaller vertebral cross-sectional dimensions; 1.47 ± 0.11 vs. 1.31 ± 0.12; P < 0.0001. Multiple linear regression analysis indicated that sex was a predictor of vertebral CSA independent of gestational age, birth weight, and body length. In contrast, sexes were monomorphic with regard to vertebral height, intervertebral disc height, and spinal length (all P's ≥ 0.11). There were also no sex differences in the length or cross-sectional dimensions of the humerus or in measures of musculature and adiposity (all P's ≥ 0.10).

Conclusions—Factors related to sex influence fetal development of the axial skeleton. The smaller vertebral CSA in females is associated with greater flexibility of the spine that could

*Corresponding Author and Reprint Requests: Vicente Gilsanz, MD, PhD, Children's Hospital Los Angeles, Department of Radiology, MS #81, 4650 Sunset Boulevard, Los Angeles, CA 90027, Phone: (323) 361-4571, Fax: (323) 361-1510, vgilsanz@chla.usc.edu.

The authors declare no conflicts of interest.

represent the human adaptation to fetal load. Unfortunately, it also imparts a mechanical disadvantage that increases stress within the vertebrae for all physical activities and the susceptibility for fragility fractures later in life.

Keywords

sexual dimorphism; vertebral fracture risk; spinal flexibility

Accumulating evidence indicates that osteoporosis has its antecedents in early childhood.[1] Recent data suggest that even the fetal environment shapes, not only one's later risk for metabolic and cardiovascular disease, but also for osteoporosis.[2] This phenomenon, known as "programming," refers to the fact that stimuli, when applied during early development, generate permanent changes that persist throughout one's lifespan. Clues that osteoporosis may result from perturbations in the fetal programming of skeletal growth come from some, but not all, epidemiological data showing a relationship between low birth weight and future risk for lower bone mass and fragility fractures.[2–5] The importance of the fetal environment to skeletal development is further supported by reports that maternal smoking, nutrition and physical activity are linked to bone mass of the offspring at birth,[6] and that placental volume and morphology are associated with neonatal bone size and mineral content.[7]

Approximately 700,000 women in the United States are newly diagnosed with vertebral fractures every year due to the inability of the vertebral body to withstand the loads associated with normal daily activities as skeletal mass and strength decline with aging. A diminished accrual of vertebral bone in girls is the basis for the lower peak bone mass (PBM) in young women, which, in turn, is a major determinant of their two- to four-fold higher incidence of vertebral fractures when compared with men.[1, 8] The basis for the lower PBM of women lay, in great part, in the smaller female vertebra because differences in vertebral bone density are less striking or nonexistent.[9–12] Women have a lower compressive vertebral strength at all ages, largely due to their smaller cross-sectional area (CSA).[10] On average, the CSA of the vertebral bodies is 25% smaller in women than in men, even after accounting for differences in body size.[9] Although the sexual dimorphism in vertebral cross-sectional dimensions is also present in early childhood,[13] the time of life when these differences first appear is currently unknown.

Our limited understanding regarding sex differences in fetal skeletal development stems from a lack of modalities to provide accurate non-invasive assessments of the three-dimensional morphology of the axial skeleton in healthy infants. Recent advances in magnetic resonance imaging (MRI) allow for fast and reliable determinations of normal newborn musculoskeletal development without the need for sedation.[14] In this study, we used MRI to test the hypothesis that sex differences in vertebral cross-sectional dimensions – a key structural determinant of the strength of the vertebra – are present at birth.

METHODS

The study population comprises of 70 white singleton full-term infants (35 male and 35 female; aged two to seven days), who were recruited from The Institute for Maternal-Fetal Health – an established alliance between the Hollywood Presbyterian Medical Center

(HPMC) and Children's Hospital Los Angeles (CHLA) between November 2013 and October 2014. The Research Oversight Committee at HPMC and the Institutional Review Board for clinical investigations at CHLA approved these studies, which were compliant with the Health Insurance Portability and Accountability Act. Written informed consent was obtained from the parent(s) of all subjects.

Only neonates born vaginally and the product of a full-term pregnancy (37–42 weeks) with a birth weight, length, and head circumference between the 10^{th} and 90^{th} percentile (according to the World Health Organization growth charts), a 1-minute Apgar score of 7 or greater and a 5-minute Apgar score of 8 or greater, and no history of cardiac, respiratory, gastrointestinal, or other systemic disease were included in this study. Infants born to mothers with a history of diabetes or gestational diabetes mellitus or the consumption of tobacco, alcohol, and illegal drugs were also excluded from this study.

MRI Measurements of Musculoskeletal Development and Adiposity

All studies were performed within one-week of age and without the use of general anesthesia and/or sedatives. Parents were instructed to keep the neonate awake as long as possible before the study and to plan a feeding (nursing or bottle) immediately prior to the scan. Then, the newborn was swaddled in cloth blankets, given protective ear muffs, and monitored with a pulse oximetry system. All subjects were examined with a 3.0 Tesla whole-body MRI scanner (Achieva R3.2, Philips Healthcare, Cleveland, Ohio) with a standard 8-channel pediatric Head/Spine coil. Subjects were scanned in the supine position. Sagittal, coronal, and axial T2-weighted images were acquired using a single shot fast spine-echo (SSFSE) sequence with 3 mm thick slices without any gap and 1 mm in-plane resolution. The repetition time ranged from 562–644 ms and the echo time ranged from 102–120 ms. Acquisition time was between 27–63 seconds.

All measurements were analyzed offline with commercial image segmentation software (SliceOmatic, Tomovision, Inc.). For the purpose of this study, the vertebral CSA, vertebral height, and intervertebral disc height were measured from the sixth thoracic to the fifth lumbar vertebrae in all newborns (Figure 1, A). Vertebral CSA determinations were obtained for a 3-mm section centered around the midpoint of each vertebral body. The length of the spine was also measured from the first cervical vertebrae to the coccyx as a proxy for truncal length. Paraspinous musculature CSA was defined as the mean of the CSAs of the erector muscles of the spine and psoas major muscle at the five lumbar vertebrae; additionally, measures of subcutaneous (SC) adiposity were obtained at the same locations (Figure 1, B). Due to the frequent flexion of the lower extremities, measures of the appendicular skeleton were obtained at the midshaft of the humerus rather than the femur. Arm musculature was defined as the sum of the cross-sectional dimensions of the biceps, triceps, and brachialis muscles at the midshaft of the humerus. The coefficients of variation for repeated MRI measurements of vertebral height and CSA, intervertebral disc height, spinal length, and truncal and arm musculature and SC adiposity were between 1.2–4.0%.

Statistical Analyses

All results are expressed as mean ± SD. Descriptive, unpaired t-test, and simple and multiple regression analyses were performed with Statview software (version 5.0.1; SAS Institute, Cary, NC). To exclude the possibility of multi-collinearity, the goodness of fit for the regression models was evaluated using the post-estimation procedures of Stata (StataCorp, College Station, TX).

RESULTS

As expected, there were no differences in the gestational age or chronological age of the newborn boys and girls. There were also no sex differences in weight, body length, or waist circumferences; although values for head circumference tended to be greater in males, this difference did not reach statistical significance. MRI measures of musculature and SC adiposity in the upper extremity or trunk did not significantly differ between sexes; females, however, tended to have less musculature and more adiposity than males at both locations (Table I).

We found that newborn girls had significantly smaller vertebral cross-sectional dimensions when compared with newborn boys of similar gestational age, weight, and body length (Table I). This was true whether the mean values for all vertebrae from T6 to L5 were compared or whether the respective values for each of the 12 vertebrae were evaluated separately (Figure 2, A). On average, the CSA of the vertebral bodies was 10.6% smaller in girls than in boys; 1.47 ± 0.11 vs. 1.31 ± 0.12 ($P < 0.0001$). Moreover, the 75^{th} percentile value for any female vertebra was below the 50^{th} percentile value for the corresponding male vertebra (Figure 2, A). In contrast, the sexes were monomorphic with regard to vertebral height, intervertebral disc height (Figure 2, B), and the length of the spine (Table I).

Multiple regression analysis indicated that the disparity in vertebral CSA between sexes was independent of gestational age, birth weight, and body length (Table II). We found that once sex and spinal length were included in the analysis, no other anthropometric or MRI measure of body composition significantly improved the predictive power of the model.

Whereas factors related to sex had a significant effect on the axial skeleton, MRI measures of the appendicular skeleton did not differ between sexes; values for both the length and cross-sectional dimensions of the humerus were similar in male and female newborns (Table I).

DISCUSSION

Available data indicate that, when compared with males, females have smaller vertebral bodies throughout childhood and young adulthood, even after accounting for differences in body size. The results of the current study provide evidence that this sexual dimorphism is present as early as at birth, and that factors related to sex are key regulators in the fetal development of the axial skeleton. The vertebral CSA of the thoracic and lumbar spine were, on average, 10.6% smaller in newborn girls than in newborn boys – a difference that was

independent of gestational age, birth weight, and body length. In contrast, the sexes were monomorphic with regard to values for vertebral height, intervertebral disc height, and spinal length.

The cross-sectional area of the vertebral body is a major determinant of its compressive strength.[9] In both males and females, values for the CSA increased from T6 to L5, consistent with their design to bear progressively larger mechanical loads as the weight of the body to be borne increases.[15] The smaller cross-sectional dimensions of the vertebral body confers a biomechanical disadvantage that increases the stress within the vertebrae throughout life and, if persists, increases the susceptibility for fragility fractures in the elderly.[9] Support for this notion comes from data showing that elderly patients with osteoporosis and vertebral fractures have significantly smaller non-fractured vertebrae than patients with a similar degree of osteoporosis who do not experience fractures in the axial skeleton.[16, 17] Indeed, vertebral size has been proposed as an independent vertebral fracture risk factor.[17]

Previous studies examining sex differences in skeletal mass at birth were limited by the inability of techniques used to assess the CSA of vertebra and yielded discrepant results. Although most found that sex had no effect on lumbar spine bone mass,[18–21] one showed that boys had higher bone mass than girls but did not account for differences in body size or examine bone morphology.[7] Using multi-planar assessments of skeletal structure, we provide new evidence for a sexual dimorphism in the intrauterine development of the axial skeleton. These results in newborns are in line with prior investigations indicating that the lower vertebral bone mass of young women when compared with men is a manifestation of early childhood differences in the size of bones.[13] Knowledge that little, if any, bone is gained from the periosteal surface of vertebral bone in adult women and the overall CSA of their vertebrae remain relatively stable underscores the importance of early variations in vertebral growth.[22, 23]

Whereas sex had a significant effect on the intrauterine development of the axial skeleton, values for humeral CSA did not differ between boys and girls at birth – consistent with existing data in children and adolescents showing that the cross-sectional dimensions of the appendicular and axial skeletons are influenced by separate determinants. Changes in the cross-sectional dimensions of the long bones in the appendicular skeleton are strongly associated with anthropometric indexes and primarily regulated by mechanical stresses, independent of sex.[24] Changes in the CSA of the vertebral body during growth are not only associated with increases in body size, but are also strongly influenced by sex.[25]

To date, there has been limited application of MRI to the study of sex differences in muscle or adipose tissue content in neonates. In the current study, females tended to have less musculature and more adiposity than males, but these differences did not reach statistical significance, likely due to the small sample size. Although an earlier study using MRI also found no substantial sex differences in total or regional body fat content at birth,[26] available data indicates that sex has a strong effect on body composition even before the onset of sexual development.[13] Sex differences in total fat content have been previously reported in large cohorts of infants using dual-energy X-ray absorptiometry.[7, 27] Further studies are

needed to better determine the degree and timing of when boys begin to accumulate significantly greater muscle but lesser fat than girls.

The mechanism(s) responsible for the smaller female vertebral body during the fetal stages of skeletal development is unknown, but likely results from complex interactions involving sex steroids, growth hormone (GH), and insulin-like growth factor.[28] Although both estrogens and androgens are important modulators of GH secretion and promote bone accretion, there are major differences in the effects of sex steroids. During adolescence, estrogens are particularly key for the regulation of epiphyseal function in both boys and girls, and higher levels in the latter lead to earlier physeal closure and a shorter appendicular skeleton by young adulthood.[29, 30] Androgens promote periosteal new bone formation, which has a dramatic effect on the width of the bone and have been implied to have a preferential effect on the growth of the axial skeleton. Observations on the treatment of children with hypopituitarism suggest that growth in the upper body segment, or trunk, is relatively more dependent on testosterone, whereas growth in the lower extremities is primarily under the control of GH.[30–32] However, the factors of relevance during fetal life that influence the sexual dimorphism in vertebral development remain unknown. Although the absence of the SRY gene in females may dictate this difference, the downstream events of importance need further investigation. Moreover, although insulin and insulin-like growth factor 2 are known regulators of fetal growth,[33] no investigations to date reveal sexual dimorphism in these values. We anticipate that careful evaluations of newborns with disorders of sex development, such as females with congenital adrenal hyperplasia, will aid in deciphering the role of androgens in mediating the fetal development of the axial skeleton. Conversely, testicular feminization syndromes may demonstrate the opposite effect, provided that estrogens and androgens influence fetal vertebral growth.

Regardless of the mechanism(s) by which sex influences intrauterine vertebral growth, it should be noted that we found no sex differences in the heights of the intervertebral discs – the fibrous cartilage tissue that act as shock absorbers with a similar size and shape as the endplates of the flanking vertebrae.[15] The height of the intervertebral disc, the compliance of its fibrous cartilage, and the dimensions of adjacent vertebrae are important determinants of spinal mobility.[15] A greater range of motion occurs when the disc is tall and/or the vertebral CSA is small.[15, 34] Thus, for comparable disc thickness and stiffness, the smaller female vertebral CSA results in greater flexion/extension and lateral flexion.[15] This notion is in agreement with anatomical and clinical studies suggesting that the lumbar spine of girls and young women have significantly greater anterior and lateral flexibility when compared with males of the same age.[35–37]

A key question is why the female fetus would be programmed with a structural characteristic that while renders her spine more flexible, also confers a higher risk for vertebral fractures later in life. A proposed explanation for the human sexual dimorphism in vertebral size could be that it improves maternal performance in posture and locomotion. The human pregnancy has some unique features relative to other mammals and requires many adaptations of the axial skeleton by virtue of the need to maintain bipedal posture. Previous comparative morphometric studies between pregnant quadrupedal chimpanzees and humans showed that human females have evolved a derived curvature and

reinforcement of the lumbar vertebrae to compensate for this bipedal obstetric load.[38] In order to counteract the shift in the center of mass associated with increases in abdominal size and weight, pregnant mothers habitually extend their lumbar spine.[39] Because greater flexibility of the spine may facilitate the lordosis needed to maintain upright posture,[38] one could hypothesize that fetal load is a selection factor in the evolution of the discrepant spinal morphology between sexes among humans.

This study showing the power of noninvasive imaging methods to examine human newborn subjects has notable limitations. Data are observational in nature and fraught with potential biases such as selection and unknown maternal variables. Although the subjects were not recruited from the community at large, any bias introduced by the method of selection would apply equally to both sexes. To facilitate homogeneity within this relatively small cohort, the sample only included vaginal deliveries of white singleton newborns between the 10th and 90th percentiles for weight and length. Moreover, beyond knowledge that they were born to mothers without a history of diabetes or gestational diabetes mellitus, information regarding highly heritable variables, such as maternal weight gain, BMI, and bone mass, were not examined. Clearly, future studies are needed to establish the generalizability of our results in other newborn populations; however, it is unlikely that these potential confounders would invalidate the large sexual dimorphism in vertebral size found in this study.

Acknowledgments

Supported by the National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases (R21DK090778).

ABBREVIATIONS

CSA	Cross-sectional area
MRI	Magnetic resonance imaging
SC	Subcutaneous

References

1. Bonjour JP, Chevalley T. Pubertal timing, bone acquisition, and risk of fracture throughout life. Endocr Rev. 2014; 35:820–47. [PubMed: 25153348]
2. Cooper C, Westlake S, Harvey N, Javaid K, Dennison E, Hanson M. Review: developmental origins of osteoporotic fracture. Osteoporos Int. 2006; 17:337–47. [PubMed: 16331359]
3. Antoniades L, MacGregor AJ, Andrew T, Spector TD. Association of birth weight with osteoporosis and osteoarthritis in adult twins. Rheumatology (Oxford). 2003; 42:791–6. [PubMed: 12730541]
4. Dennison EM, Syddall HE, Sayer AA, Gilbody HJ, Cooper C. Birth weight and weight at 1 year are independent determinants of bone mass in the seventh decade: the Hertfordshire cohort study. Pediatr Res. 2005; 57:582–6. [PubMed: 15695596]
5. Byberg L, Michaelsson K, Goodman A, Zethelius B, Koupil I. Birth Weight is not Associated With Risk of Fracture: Results from Two Swedish Cohort Studies. J Bone Miner Res. 2014; 29:2152–60. [PubMed: 24723393]
6. Godfrey K, Walker-Bone K, Robinson S, Taylor P, Shore S, Wheeler T, et al. Neonatal bone mass: influence of parental birthweight, maternal smoking, body composition, and activity during pregnancy. J Bone Miner Res. 2001; 16:1694–703. [PubMed: 11547840]

7. Holroyd CR, Harvey NC, Crozier SR, Winder NR, Mahon PA, Ntani G, et al. Placental size at 19 weeks predicts offspring bone mass at birth: findings from the Southampton Women's Survey. Placenta. 2012; 33:623–9. [PubMed: 22640438]
8. Hernandez CJ, Beaupre GS, Carter DR. A theoretical analysis of the relative influences of peak BMD, age-related bone loss and menopause on the development of osteoporosis. Osteoporos Int. 2003; 14:843–7. [PubMed: 12904837]
9. Gilsanz V, Boechat MI, Gilsanz R, Loro ML, Roe TF, Goodman WG. Gender differences in vertebral sizes in adults: biomechanical implications. Radiology. 1994; 190:678–82. [PubMed: 8115610]
10. Bouxsein ML, Melton LJ 3rd, Riggs BL, Muller J, Atkinson EJ, Oberg AL, et al. Age- and sex-specific differences in the factor of risk for vertebral fracture: a population-based study using QCT. J Bone Miner Res. 2006; 21:1475–82. [PubMed: 16939406]
11. Fournier PE, Rizzoli R, Slosman DO, Buchs B, Bonjour JP. Relative contribution of vertebral body and posterior arch in female and male lumbar spine peak bone mass. Osteoporos Int. 1994; 4:264–72. [PubMed: 7812074]
12. Kalender WA, Felsenberg D, Louis O, Lopez P, Klotz E, Osteaux M, et al. Reference values for trabecular and cortical vertebral bone density in single and dual-energy quantitative computed tomography. Eur J Radiol. 1989; 9:75–80. [PubMed: 2743986]
13. Arfai K, Pitukcheewanont PD, Goran MI, Tavare CJ, Heller L, Gilsanz V. Bone, muscle, and fat: sex-related differences in prepubertal children. Radiology. 2002; 224:338–44. [PubMed: 12147825]
14. Laor T, Jaramillo D. MR imaging insights into skeletal maturation: what is normal? Radiology. 2009; 250:28–38. [PubMed: 19092089]
15. Middleditch, A.; Oliver, J. Normal Movement. In: Middleditch, A.; Oliver, J., editors. Functional Anatomy of the Spine. 2. Butterworth Heinemann; 2005. p. 173-208.
16. Gilsanz V, Loro ML, Roe TF, Sayre J, Gilsanz R, Schulz EE. Vertebral size in elderly women with osteoporosis. Mechanical implications and relationship to fractures. J Clin Invest. 1995; 95:2332–7. [PubMed: 7738196]
17. Ruyssen-Witrand A, Gossec L, Kolta S, Dougados M, Roux C. Vertebral dimensions as risk factor of vertebral fracture in osteoporotic patients: a systematic literature review. Osteoporos Int. 2007; 18:1271–8. [PubMed: 17340217]
18. Koo WW, Hockman EM. Physiologic predictors of lumbar spine bone mass in neonates. Pediatr Res. 2000; 48:485–9. [PubMed: 11004239]
19. Namgung R, Tsang RC. Factors affecting newborn bone mineral content: in utero effects on newborn bone mineralization. Proc Nutr Soc. 2000; 59:55–63. [PubMed: 10828174]
20. Ahmad I, Nemet D, Eliakim A, Koeppel R, Grochow D, Coussens M, et al. Body composition and its components in preterm and term newborns: A cross-sectional, multimodal investigation. Am J Hum Biol. 2010; 22:69–75. [PubMed: 19533616]
21. Salle BL, Braillon P, Glorieux FH, Brunet J, Cavero E, Meunier PJ. Lumbar bone mineral content measured by dual energy X-ray absorptiometry in newborns and infants. Acta Paediatr. 1992; 81:953–8. [PubMed: 1290856]
22. Mosekilde L. Sex differences in age-related changes in vertebral body size, density and biomechanical competence in normal individuals. Bone. 1990; 11:67–73. [PubMed: 2357425]
23. Wren TA, Kim PS, Janicka A, Sanchez M, Gilsanz V. Timing of peak bone mass: discrepancies between CT and DXA. J Clin Endocrinol Metab. 2007; 92:938–41. [PubMed: 17164299]
24. van der Meulen MC, Beaupre GS, Carter DR. Mechanobiologic influences in long bone cross-sectional growth. Bone. 1993; 14:635–42. [PubMed: 8274306]
25. Gilsanz V, Kovanlikaya A, Costin G, Roe TF, Sayre J, Kaufman F. Differential effect of gender on the sizes of the bones in the axial and appendicular skeletons. J Clin Endocrinol Metab. 1997; 82:1603–7. [PubMed: 9141557]
26. Harrington TA, Thomas EL, Modi N, Frost G, Coutts GA, Bell JD. Fast and reproducible method for the direct quantitation of adipose tissue in newborn infants. Lipids. 2002; 37:95–100. [PubMed: 11878317]

27. Koo WW, Walters JC, Hockman EM. Body composition in human infants at birth and postnatally. J Nutr. 2000; 130:2188–94. [PubMed: 10958811]
28. Kawai M, Rosen CJ. The IGF-I regulatory system and its impact on skeletal and energy homeostasis. J Cell Biochem. 2010; 111:14–9. [PubMed: 20506515]
29. Acherman, JC.; Hughes, IA. Disorders of Sex Development. In: Melmed, S.; Polonsky, KS.; Larsen, PR.; Kronenberg, HM., editors. Williams Textbook of Endocrinology. 12. Philadelphia: Elsevier Inc; 2011. p. 868-934.
30. Tanner JM, Whitehouse RH, Hughes PC, Carter BS. Relative importance of growth hormone and sex steroids for the growth at puberty of trunk length, limb length, and muscle width in growth hormone-deficient children. J Pediatr. 1976; 89:1000–8. [PubMed: 993900]
31. Aynsley-Green A, Zachmann M, Prader A. Interrelation of the therapeutic effects of growth hormone and testosterone on growth in hypopituitarism. J Pediatr. 1976; 89:992–9. [PubMed: 993931]
32. Ross JL, Quigley CA, Cao D, Feuillan P, Kowal K, Chipman JJ, et al. Growth hormone plus childhood low-dose estrogen in Turner's syndrome. N Engl J Med. 2011; 364:1230–42. [PubMed: 21449786]
33. Hiden U, Glitzner E, Hartmann M, Desoye G. Insulin and the IGF system in the human placenta of normal and diabetic pregnancies. J Anat. 2009; 215:60–8. [PubMed: 19467150]
34. Kim HJ, Yeom JS, Lee DB, Kang KT, Chang BS, Lee CK. Association of benign joint hypermobility with spinal segmental motion and its clinical implication in active young males. Spine. 2013; 38:E1013–9. [PubMed: 23846448]
35. Haley SM, Tada WL, Carmichael EM. Spinal mobility in young children. A normative study. Phys Ther. 1986; 66:1697–703. [PubMed: 3774880]
36. Penha PJ, Casarotto RA, Sacco ICN, Marques AP, João SMA. Qualitative postural analysis among boys and girls of seven to ten years of age. Rev Bras Fisioter. 2008; 12:386–91.
37. Twomey, LT.; Taylor, JR. Lumbar posture, movement and mechanics. In: Twomey, LT.; Taylor, JR., editors. Physical Therapy of the Low Back. Edinburgh: Churchill Livingstone; 1987. p. 51-84.
38. Whitcome KK, Shapiro LJ, Lieberman DE. Fetal load and the evolution of lumbar lordosis in bipedal hominins. Nature. 2007; 450:1075–8. [PubMed: 18075592]
39. Jensen RK, Doucet S, Treitz T. Changes in segment mass and mass distribution during pregnancy. J Biomech. 1996; 29:251–6. [PubMed: 8849820]
40. Dowthwaite JN, Rosenbaum PF, Scerpella TA. Mechanical loading during growth is associated with plane-specific differences in vertebral geometry: A cross-sectional analysis comparing artistic gymnasts vs. non-gymnasts. Bone. 2011; 49:1046–54. [PubMed: 21839871]

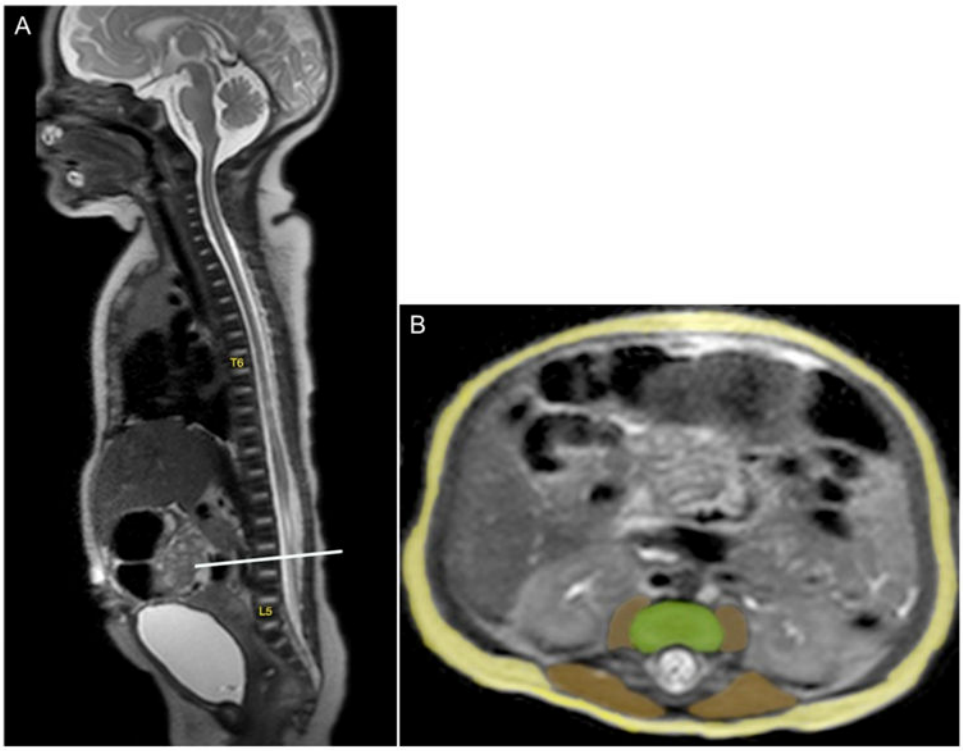

Figure 1. MRI images of the spine in a 3-day old newborn

(A) Coned-down sagittal T2-weighted SSFSE image of the spine showing the vertebral bodies and intervertebral discs, labels at T6 and L5, and the location (white line) of (B) the axial T2-weighted SSFSE image outlining the vertebral body (green), paraspinous musculature (brown), and subcutaneous adiposity (yellow).

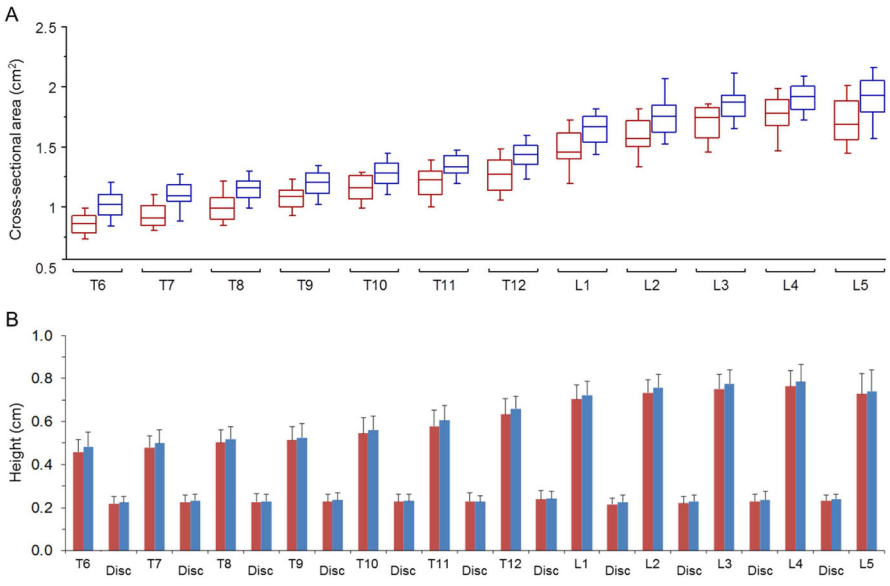

Figure 2. Spinal dimensions in newborns

(A) Box plots of MRI vertebral CSA values from T6 to L5 in 35 boys (blue) and 35 girls (red), showing significantly smaller female mean cross-sectional area at all locations; all P's ≤ 0.008. (B) Bar plots of vertebral and intervertebral disc heights in the same newborns showing similar values between males and females; all P's ≥ 0.085. Values are expressed as mean ± SD.

Table I

Ages, anthropometric measures, and MRI measures of fat, muscle, and bone in 70 healthy newborns.

	Males *(n = 35)*	Females *(n = 35)*	P-value
Gestational Age (wk)	38.9 ± 1.17	39.0 ± 1.21	0.721
Age (day)	2.94 ± 1.43	3.43 ± 1.87	0.227
Weight (kg)	3.38 ± 0.42	3.26 ± 0.40	0.215
Body length (cm)	50.6 ± 2.39	50.4 ± 2.73	0.743
Head circumference (cm)	34.0 ± 1.31	33.4 ± 1.41	0.060
Waist Circumference (cm)	30.8 ± 1.47	30.7 ± 2.05	0.827
Appendicular skeleton			
Arm SC adiposity (cm^2)	4.95 ± 1.13	5.16 ± 1.10	0.422
Arm musculature (cm^2)	3.38 ± 0.68	3.19 ± 0.66	0.222
Humeral length (cm)	8.18 ± 0.37	8.05 ± 0.40	0.151
Humeral CSA (cm^2)	0.37 ± 0.07	0.35 ± 0.08	0.386
Axial Skeleton			
Abdominal SC adiposity (cm^2)	11.4 ± 1.85	11.8 ± 2.25	0.439
Paraspinous musculature (cm^2)	4.10 ± 0.68	3.85 ± 0.58	0.102
Spinal length (cm)	23.6 ± 1.22	23.1 ± 1.22	0.108
Intervertebral disc height (cm)	0.23 ± 0.02	0.23 ± 0.03	0.323
Vertebral Height (cm)	0.64 ± 0.06	0.62 ± 0.06	0.151
Vertebral CSA (cm^2)	1.47 ± 0.11	1.31 ± 0.12	<0.0001

Table II

Multiple regression model of measures for vertebral CSA in 70 newborns with gestational age, sex, weight and length as independent variables.

	β	SE	P-value	R^2
Vertebral CSA				0.372
Gestational age (wk)	−0.092	0.015	0.468	
Sex	−0.550	0.028	<0.0001	
Weight (kg)	0.003	0.047	0.983	
Length (cm)	0.272	0.008	0.056	