Normal Growth and Development of Fetal External Genitalia Demonstrated by Sonography

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ABSTRACT: *Purpose.* Our aim in this retrospective sonographic study was to describe the normal growth and development of fetal external genitalia.

Methods. We reviewed the sonograms of anatomically normally fetuses, obtained over a 5-year period, and measured transverse scrotal diameter or penile length in male fetuses and bilabial diameter in female fetuses. Transverse scrotal diameter was measured from the midpoint of the lateral scrotal wall to the midpoint of the opposite lateral wall; penile length, from the base of the shaft to the tip; and bilabial diameter, from the midpoint of the lateral labial margin to the midpoint of the opposite lateral labial margin.

Results. We examined sonograms from 1,182 fetuses and measured transverse scrotal diameter in 304 and penile length in 494 male fetuses and bilabial diameter in 384 female fetuses. The fetuses ranged from 14 to 41 weeks' menstrual age. Transverse scrotal diameter, penile length, and bilabial measurements were highly correlated with menstrual age ($r = 0.941$, $r = 0.860$, and $r = 0.898$, respectively). We found that growth of fetal external genitalia is similar to that for other parameters of fetal growth, such as biparietal diameter and femur length.

Conclusions. The results of this study may be helpful in understanding the natural course of the growth and development of fetal external genitalia. In addition, the data we gathered may be useful in combination with other biometric data for estimating fetal age and may help in detecting abnormalities in the fetal external genitalia. *J Clin Ultrasound* **31**:465–472, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/jcu.10207

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A search of the English-language medical literature yielded no articles documenting progressive changes in genital growth and the prenatal sonographic appearance of the genitalia, with the exception of several reports on development of the fetal penis.[1,2] Our study was designed to prospectively observe normal penile length, transverse scrotal and bilabial diameter growth, and external genitalia morphologic development using prenatal diagnostic sonography. An understanding of the normal growth patterns may be helpful in detecting abnormalities of fetal external genitalia.

PATIENTS AND METHODS

In this cross-sectional retrospective study, we reviewed all sonograms obtained over a 5-year period during prenatal sonographic examinations at our institution. All fetuses had been examined by registered diagnostic sonographers using HDI 3000, HDI 5000, or Ultramark 9 ultrasound scanners (Philips-ATL, Bothell, WA). In male fetuses, we measured transverse scrotal diameter or penile length, and in female fetuses, bilabial diameter. All scans and measurements were reviewed by a maternal–fetal medicine specialist, and the single best measurement was recorded. In addition, the anatomic structure of all external fetal genitalia was observed; only fetuses with normal anatomy were included in the study. Because it was retrospective, this study received exempt status from the Maine Medical Center institutional review board.

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The gestational age of each fetus was determined from the date of the mother's last menstrual period. However, if menstrual dating was uncertain or there was a discrepancy of more than 2 weeks between the last menstrual period dating and the sonographic dating, we used the sonographically determined age, which was estimated from the measurements of the biparietal diameter, head circumference, bicerebellar diameter, outer orbital diameter, humerus length, femur length, fibula length, tibia length, foot length, and abdominal circumference.

All measurements for this study were made by experienced sonographers. The transverse scrotal diameter was measured from the midpoint of the lateral scrotal wall to the midpoint of the opposite lateral wall. The standard plane was obtained at the widest cross section or coronal section of the scrotum (Figure 1). Penile length was measured from the base of the shaft to the tip of the penis. The bilabial diameter was measured from the midpoint of the lateral labial margin to the midpoint of the opposite lateral labial margin. The standard plane was obtained at the widest cross section or coronal section of the labia (Figure 2). Clitoral length measurement had been included in the initial study design but was not obtainable in most of the female fetuses, so that parameter was excluded from study.

Standard deviations (SDs) were calculated using StatView software (SAS Institute, Cary, NC) on a Macintosh computer. CA-Cricket Graph III software (Computer Associates International, Islandia, NY) was used to generate best-fit curves as well as +1.96 and −1.96 SD curves.

RESULTS

We reviewed sonograms from a total of 1,182 fetuses from a predominantly white, middle-class population in the state of Maine. The fetuses ranged from 14 to 41 weeks' menstrual or sonographically determined age. Transverse scrotal diameter was measured in 304 fetuses, penile length in 494, and bilabial diameter in 384.

External Genital Development in Male Fetuses

Transverse Scrotal Diameter. Statistical analysis showed that transverse scrotal measurements were highly correlated with menstrual age with a third-degree polynomial pattern ($r = 0.941$, $r^2 = 0.885$, standard error of estimate = 0.343, $p < 0.0001$). The development of transverse scrotal diameter by fetal age was obtained with the formula menstrual age in weeks = 8.16 + (17.47 × transverse scrotal diameter in cm) − [4.35 × (transverse scrotal diameter in cm)^2] + [0.50 × (transverse scrotal diameter in cm)^3].

The mean transverse scrotal diameters and the transverse scrotal diameters + 1.96 and −1.96 SDs for the fetuses are shown in Table 1. The SD, representing individual variation, increased as fetal age increased, from 0.10 cm at 14 weeks to 0.44 cm at 41 weeks. Transverse scrotal diameter gradually

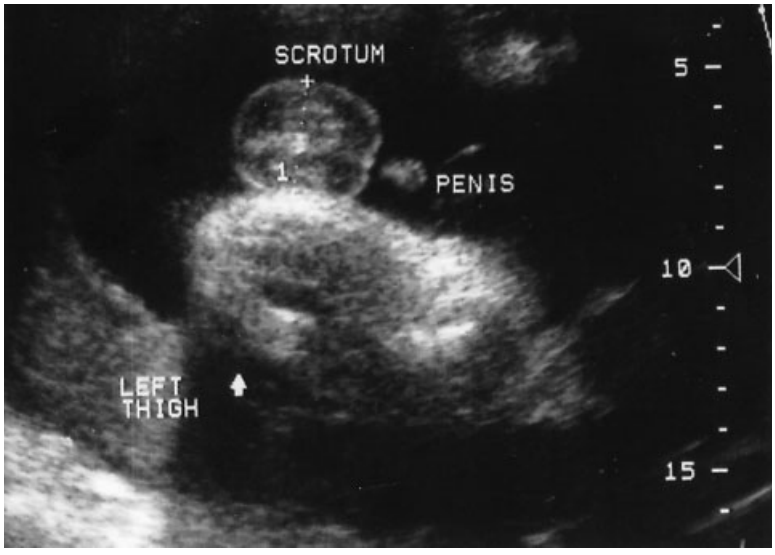

FIGURE 1. Transverse sonogram illustrates the plane used for measuring fetal transverse scrotal diameter in the third trimester. Calipers are positioned on the lateral edges of the scrotal sac at its widest dimension. The scrotum, containing the testicles, is visible, as are the penis and the left thigh.

FIGURE 2. Transverse sonogram illustrates the plane used for measuring fetal bilabial diameter in the third trimester. Calipers are positioned on the lateral edges of the labia majora.

increased from 0.07 cm/week at 14 weeks to about 0.2 cm/week after 32 weeks until term. The curve of fetal transverse scrotal diameters versus menstrual age is shown in Figure 3.

Penile Length. Penile length also showed a close correlation with gestational age ($r = 0.860$, $r^2 = 0.735$, standard error of estimate = 2.92, $p < 0.0001$). Penile growth with increasing age had a second-degree polynomial pattern with the formula menstrual age in weeks = 8.2769 + (16.9680 × penile length in cm) − (1.4038 × penile length in cm)^2. The weekly mean values and SDs

TABLE 1
Transverse Scrotal Diameter, Penile Length, and Bilabial Diameter Measurements in 1,182 Anatomically Normal Fetuses

Menstrual Age, weeks	Transverse Scrotal Diameter, cm ($n = 304$)				Penile Length, cm ($n = 494$)				Bilabial Diameter, cm ($n = 384$)			
	−1.96 SD	Mean	+1.96 SD	SD	−1.96 SD	Mean	+1.96 SD	SD	−1.96 SD	Mean	+1.96 SD	SD
14	0.17	0.37	0.57	0.10	—	—	—	—	0.08	0.24	0.40	0.08
15	0.22	0.44	0.66	0.11	—	—	—	—	0.13	0.29	0.45	0.08
16	0.29	0.51	0.73	0.11	—	—	—	—	0.18	0.35	0.52	0.09
17	0.34	0.58	0.82	0.12	0.34	0.54	0.74	0.10	0.23	0.40	0.57	0.09
18	0.40	0.67	0.94	0.14	0.36	0.60	0.84	0.12	0.28	0.46	0.64	0.09
19	0.46	0.75	1.04	0.15	0.40	0.67	0.94	0.14	0.33	0.52	0.71	0.10
20	0.52	0.83	1.14	0.16	0.42	0.73	1.04	0.16	0.37	0.59	0.81	0.11
21	0.58	0.93	1.28	0.18	0.46	0.80	1.14	0.18	0.41	0.65	0.89	0.12
22	0.65	1.02	1.39	0.19	0.49	0.87	1.25	0.19	0.45	0.72	0.99	0.14
23	0.73	1.12	1.51	0.20	0.52	0.94	1.36	0.21	0.50	0.79	1.08	0.15
24	0.82	1.23	1.64	0.21	0.56	1.01	1.46	0.23	0.54	0.86	1.18	0.16
25	0.89	1.34	1.79	0.23	0.59	1.08	1.57	0.25	0.59	0.93	1.27	0.17
26	0.99	1.46	1.93	0.24	0.63	1.15	1.67	0.27	0.65	1.01	1.37	0.19
27	1.10	1.59	2.08	0.25	0.67	1.23	1.79	0.29	0.72	1.10	1.48	0.19
28	1.20	1.73	2.26	0.27	0.70	1.30	1.90	0.30	0.77	1.18	1.59	0.21
29	1.33	1.88	2.43	0.28	0.75	1.38	2.01	0.32	0.84	1.27	1.70	0.22
30	1.47	2.04	2.61	0.29	0.79	1.46	2.13	0.34	0.91	1.37	1.83	0.23
31	1.60	2.21	2.82	0.31	0.83	1.53	2.23	0.36	0.99	1.47	1.95	0.25
32	1.77	2.40	3.03	0.32	0.87	1.61	2.35	0.38	1.07	1.58	2.09	0.26
33	1.94	2.59	3.24	0.33	0.91	1.69	2.47	0.40	1.17	1.70	2.23	0.27
34	2.12	2.79	3.46	0.34	0.97	1.78	2.59	0.41	1.27	1.82	2.37	0.28
35	2.28	2.99	3.70	0.36	1.01	1.86	2.71	0.43	1.35	1.95	2.55	0.31
36	2.46	3.19	3.92	0.37	1.07	1.95	2.83	0.45	1.45	2.10	2.75	0.33
37	2.64	3.38	4.12	0.38	1.12	2.04	2.96	0.47	1.57	2.26	2.95	0.35
38	2.78	3.56	4.34	0.40	1.17	2.13	3.09	0.49	1.69	2.42	3.15	0.37
39	2.94	3.74	4.54	0.41	1.23	2.22	3.21	0.51	1.84	2.60	3.36	0.39
40	3.06	3.88	4.70	0.42	1.28	2.31	3.34	0.53	2.00	2.80	3.60	0.41
41	3.22	4.08	4.94	0.44	1.35	2.41	3.47	0.54	2.18	3.03	3.88	0.43

Abbreviation: SD, standard deviation.

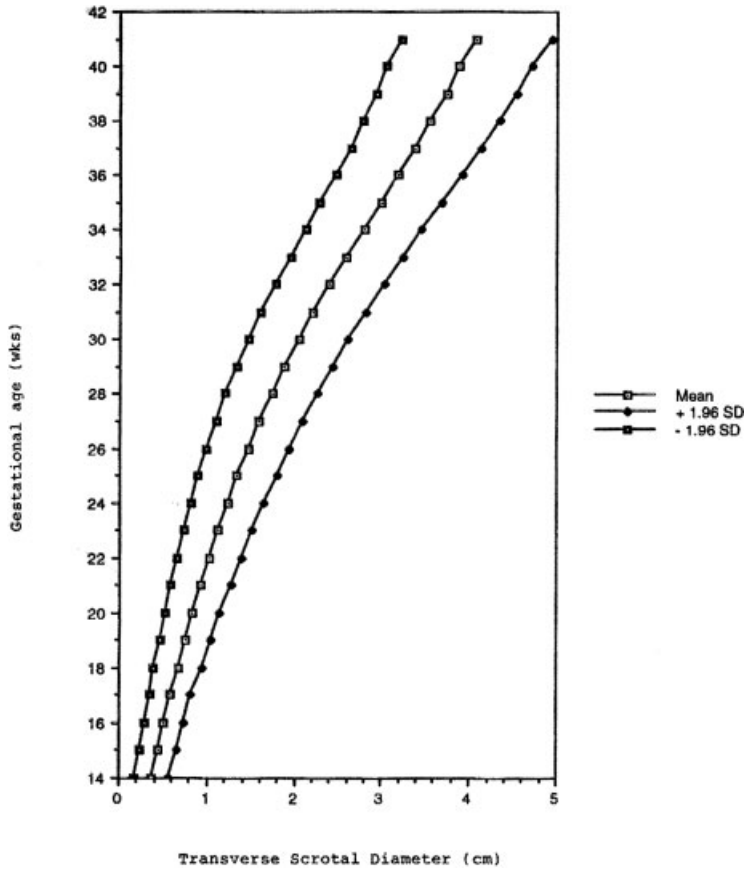

FIGURE 3. Graph shows the growth curve for the transverse scrotal diameter with increasing fetal age.

for penile length are presented in Table 1, and its development curve is shown in Figure 4.

Sonographic Visualization of Morphologic Changes. In addition to an increase in size of the external genitalia, morphologic changes were also observed with increasing fetal age. From 11 to 14 weeks' menstrual age, the scrotum appeared as a small semicircular structure, and the penis could be identified protruding from the midline, but the testicles could not be identified (Figure 5). After 14 to 15 weeks, the scrotum became more protuberant and rounded, with the penis protruding from the midline; occasionally the testicles could be identified within the scrotal sac. After 28 weeks, the scrotum became less echogenic and was often seen to be not as round as it had appeared earlier in the pregnancy; the penis could be identified protruding from the midline, and the testicles were usually seen within the scrotum (Figure 1).

External Genital Development in Female Fetuses

Bilabial Diameter. Statistical analysis revealed a significant correlation between bilabial diameter and fetal age in a third-degree polynomial pattern ($r = 0.898$, $r^2 = 0.806$, standard error of estimate = 0.255, $p < 0.0001$). A formula for the bilabial diameter growth curve was established as follows: menstrual age in weeks = 9.2795 + (21.1240 × bilabial diameter in cm) − [5.0924 × (bilabial diameter in cm)^2] + [0.5204 × (bilabial diameter in cm)^3].

The mean bilabial diameters and the bilabial diameters +1.96 and −1.96 SDs for the fetuses are shown in Table 1. The SD, representing individual variation, also increased as fetal age increased, from 0.08 cm at 14 weeks to 0.43 cm at 41 weeks. Bilabial diameter increased by 0.05–0.07 cm/week from 14 to 27 weeks. The rate of growth increased gradually after 28 weeks, reaching 0.20 cm/week at term. The curve of fetal bilabial diameters versus menstrual age is shown in Figure 6.

Sonographic Visualization of Morphologic Changes. From 13 to 16 weeks' menstrual age, the labia and clitoris appeared as 3 small parallel echogenic lines (Figure 7). During the second trimester, the parallel echogenic lines could still be appreciated, but their surfaces appeared more rounded than they had earlier. During the late second and third trimesters, the labia and clitoris could be identified as 3 bumps, with the clitoris protruding from the midline (Figure 2).

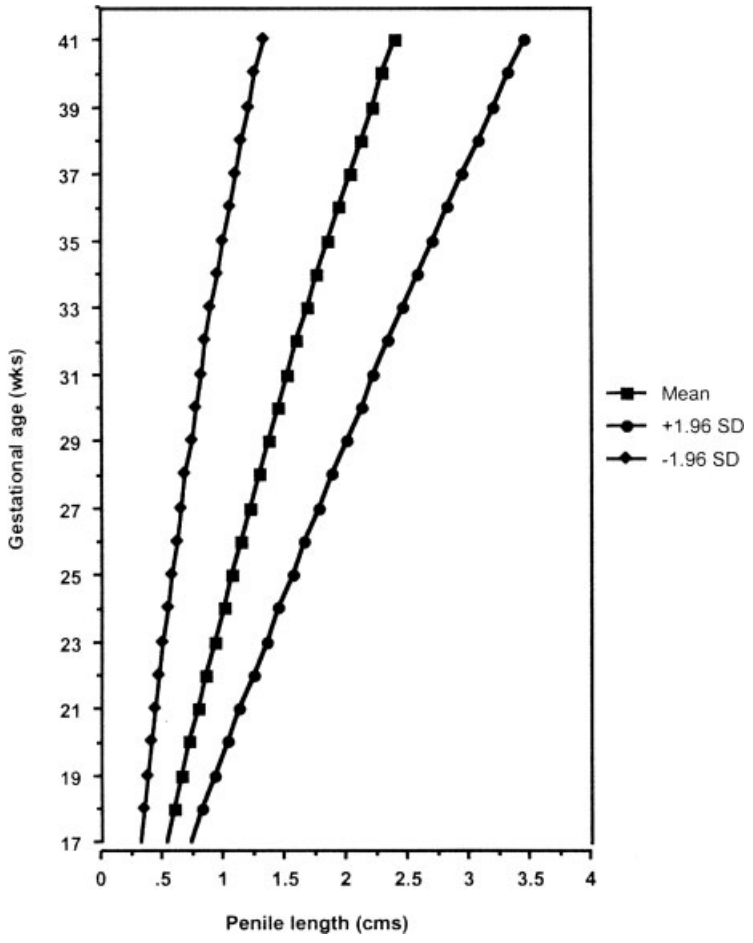

FIGURE 4. Graph shows the growth curve for penile length with increasing fetal age.

FIGURE 5. Transverse sonogram shows an early second-trimester male fetus's external genitalia, with the penis identified protruding from the midline (calipers).

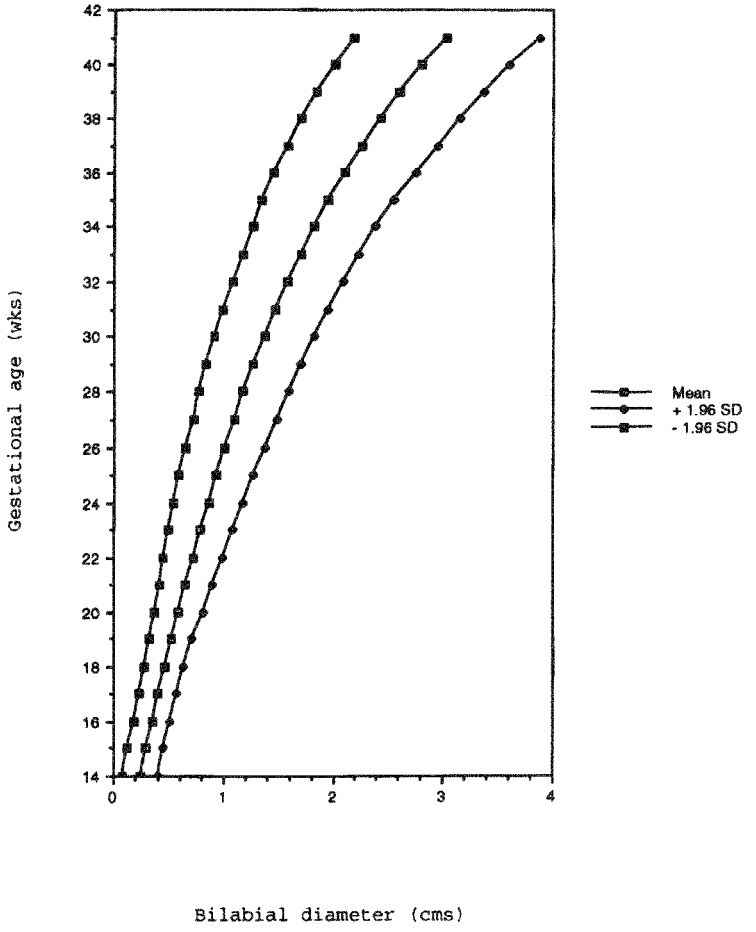

FIGURE 6. Graph shows the growth curve for bilabial diameter with increasing fetal age.

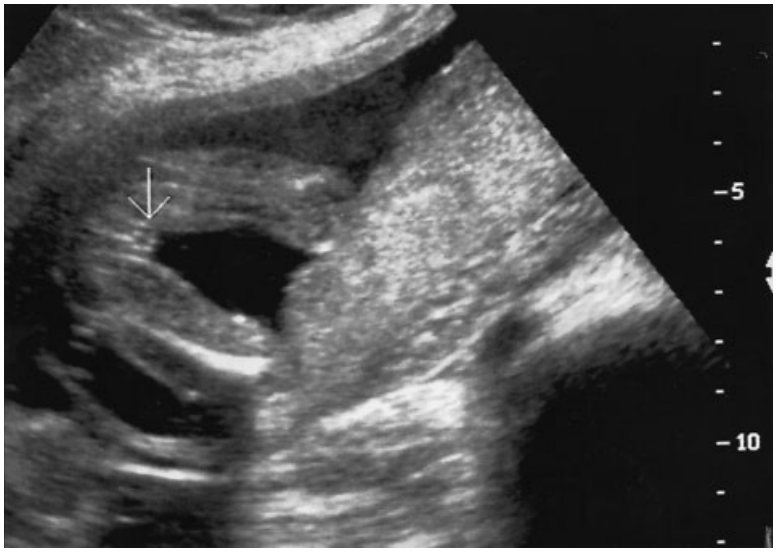

FIGURE 7. Transverse sonogram shows an early second-trimester female fetus's external genitalia, visualized as 3 small parallel echogenic lines (arrow).

DISCUSSION

Development of the reproductive tract begins in the sixth week of the embryonic period, and external genitalia develop during the eighth to fourteenth weeks of gestation.[3] External determination of sex is not possible before urogenital sinus remodeling is complete, which also occurs between the eighth and fourteenth weeks.

Advances in sonography now permit visualization of fetal genitalia that previously eluded consistent identification. Using the midsagittal plane, sonographic determination of fetal sex has been reported as early as 11 weeks' menstrual age, but it may be obtained reliably only as early as 12 to 13 weeks.[4–8] Early identification of fetal sex appears to require a great deal of operator experience to obtain a correct sagittal reference plane, and the accuracy rate is limited by fetal age, improving as menstrual age advances from 75% at 12 weeks to 90% at 14 weeks. The transverse plane can be used effectively after 14 weeks, and with a combination of tangential or transverse and sagittal views, fetal sex can be determined 93% of the time, with an accuracy of 99%, after 14 weeks' menstrual age.[9]

Distinguishing between a small penis and a prominent clitoris and between minimally edematous labia and a small scrotum filled with spongy connective tissue may be difficult at the start of the second trimester. In our experience, visualization of the genital area is totally dependent on fetal position, and the best images are obtained on a tangential plane through the genital area after 14 weeks. Three errors are common. First, the umbilical cord can be confused with either male or female genitalia, depending on its position between the femurs. Second, the scrotal sac may contain widely spaced testes, resembling separated labial swellings, instead of appearing as a sac containing 2 testes lying closely side by side. Third, determination of fetal sex may not be possible even with clear visualization of both the labia and the clitoris or the scrotum and the penis.

We found that the growth of fetal external genitalia is similar to that for other parameters of fetal growth, such as biparietal diameter and femur length.[10,11] Variations of the fetal external genitalia in terms of size, spacing, and definition are similar to the variations observed in infant populations, presumably reflecting sexually associated hormonal effects.[12,13]

Documentation of fetal sex and normal development of the genitalia can be clinically important and should not be done only to satisfy idle parental curiosity. Bronshtein[14] has reported the possible sonographic diagnoses of fetal genital anomalies. The identification of fetal sex has been helpful in the differentiation of monozygosity or dizygosity in twin pregnancy.[15] And careful examination of the fetal perineum may detect fetal genital malformations that can often be associated with various syndromes (eg, Opitz syndrome, Bardet-Biedl syndrome)[16] or chromosomal abnormalities (eg, triploidy). Furthermore, cases with a discrepancy between sonographic and chromosomal sex identification may indicate the presence of testicular feminization or congenital adrenal hyperplasia.[17] For pregnancies at risk for X-linked disorders, demonstrating a female fetus excludes the possibility of the disorder.[15] Abnormally large or small fetal external genitalia may indicate hypergonadism, hypogonadism, external genital malformations, and intersex conditions (for example, microphallus as part of congenital hypopituitarism). In the case of cryptorchidism, the transverse scrotal diameter may be smaller than normal in addition to the absence of testes and the presence of a small penis. Ambiguous genitalia may appear as either a larger than normal bilabial diameter or a smaller than normal transverse scrotal diameter and penile length. In addition, a larger than normal transverse scrotal diameter or bilabial diameter may be seen in fetuses with a hydrocele or edema of the labia majora. Finally, a larger than normal scrotum has been seen in fetuses with an inguinal hernia.[18]

Conducting this retrospective sonographic study in 1,182 fetuses with normal anatomy allowed us to provide potentially useful clinical information that is currently missing from the English-language medical literature. Our results should help increase clinicians' understanding of the normal growth and development of fetal external genitalia, provide data that can be used in combination with other biometric data to estimate fetal age, and be useful in detecting abnormalities of fetal external genitalia.

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