Ovarian and Uterine Sonography in Healthy Girls Between 1 and 13 Years Old: Correlation of Findings with Age and Pubertal Status

Liliane Diefenthaeler Herter[1]
Eliete Golendziner[2]
José Antônio Monteiro Flores[2]
Eduardo Becker, Jr.[3]
Poli Mara Spritzer[1]

OBJECTIVE. Our objective was to correlate ovarian and uterine sonographic variables with age and pubertal status in a sample of healthy girls.

SUBJECTS AND METHODS. In this prospective study, 139 consecutive patients between 1 and 13 years old (mean ± SD, 6.0 ± 3.4 years) underwent sonography and hand radiography (for bone-age determination). Pubertal development was classified according to Tanner stages (prepubertal, 5.0 ± 2.7 years [n = 117]; pubertal, 11.2 ± 1.2 years [n = 22]). Uterine and ovarian longitudinal, transverse, and anteroposterior diameters were measured. Uterine fundal–cervical ratio was determined. Ovaries were morphologically classified as homogeneous, paucicystic, multicystic, macrocystic, and presenting isolated cysts. A p value less than or equal to 0.05 was considered significant.

RESULTS. The uterus was identified in 96% of the patients (mean, 6.1 ± 3.4 years). One ovary was visible in 93% (mean, 6.2 ± 3.4 years), and both ovaries, in 81% (mean, 6.5 ± 3.3 years). Neither ovary was visualized in 10 girls (mean, 2.5 ± 2.2 years). Uterine parameters and ovarian volume were smaller in patients without thelarche ($p < 0.0001$). Mean ovarian and uterine size was smaller in girls until 8 years, intermediate between 9 and 11 years, and larger after 12 years ($p < 0.0001$). Chronologic age, bone age, and Tanner stage were correlated even before 7 years. Patients with and without thelarche presented different ovarian morphology ($p = 0.01$).

CONCLUSION. Uterine and ovarian growth was associated with age and puberty. Uterine length presented the best correlation with age. Multicystic ovaries seemed to be correlated with normal or premature pubertal stimuli.

Sonography is a noninvasive and painless technique used for assessing pelvic disorders in children and adolescents [1]. This low-risk procedure has been used to evaluate patients with ambiguous genitalia, pelvic tumors, late or premature puberty, and pelvic pain [2, 3].

Although sonography is routinely performed, there is a wide variation in the results of several studies concerning sonographic pelvic findings in children and adolescents. Uterine and ovarian growth patterns during infancy and puberty are not completely understood; also, no consensus exists about the normal measures and morphologic appearance of the ovaries. This may be attributed to the methodologic limitations of most studies, such as inclusion of both pubertal and prepubertal girls in the same analysis [4], small populations [5–7], absence of prepubertal girls younger than 8 years from the analyses [4, 8, 9], lack of statistical analyses [4, 5, 7], and use of formulae associated with logarithmic transformation, the application of which is not practical [10]. In addition, although cystic ovarian structures are also commonly observed on sonography, the classification of these structures is confusing and nonuniform. Investigators use either identical terms for different concepts or different terms for identical concepts, making the comparison among studies more difficult. For these reasons, physicians often do not know how to interpret sonographic results.

The aim of our study was to correlate ovarian volume, ovarian morphology, uterine volume, uterine area, and uterine length as observed on sonography with chronologic age, bone age, and breast pubertal status (Tanner scale [11]) in a sample of healthy girls.

Subjects and Methods

Our study included girls between 1 and 13 years old (mean ± SD, 6.0 ± 3.4 years; median, 6 years)

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[1]Gynecological Endocrinology Unit, Division of Endocrinology, Hospital de Clínicas de Porto Alegre, Avenida Ramiro Barcelos 2350, 90035-903, Porto Alegre, Brazil. Address correspondence to L. D. Herter.

[2]Radiology Service, Hospital da Criança Santo Antônio, Avenida Ceará 1549, 90240-512, Porto Alegre, Brazil.

[3]Graduate Program in Clinical Medicine, Universidade Federal do Rio Grande do Sul. Avenida Ramiro Barcelos 2350, 90035-903, Porto Alegre, Brazil.

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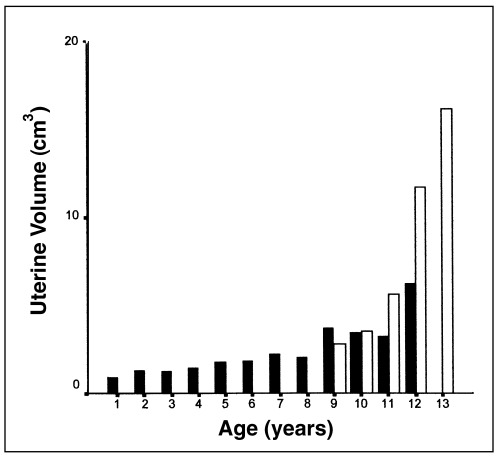

Fig. 1.—Bar chart shows uterine volume in patients without thelarche (1.8 ± 1.2 cm^3) (black bar) and with thelarche (8.1 ± 6.6 cm^3) (white bar) (Mann-Whitney test, $p < 0.0001$).

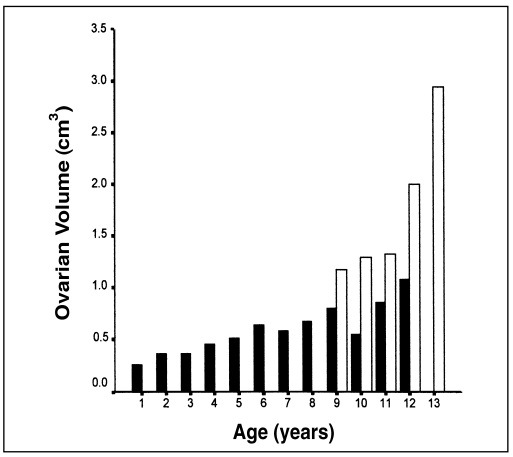

Fig. 2.—Bar chart shows ovarian volume in patients without thelarche (0.5 ± 0.3 cm^3) (black bar) and with thelarche (1.7 ± 1.2 cm^3) (white bar) (Mann-Whitney test, $p < 0.0001$). In the group between 9 and 12 years old, a statistically significant difference in ovarian volume was observed when comparing patients with and without thelarche (Mann-Whitney test, $p = 0.014$).

referred to the Radiology Service at Hospital da Criança Santo Antônio, a tertiary care hospital (Porto Alegre, Brazil), for investigation of urinary infection or abdominal discomfort between August 1998 and April 1999. Girls presenting gynecologic or endocrine disorders, severe or weakening conditions, urogynecologic malformation or pelvic pain, and those who had the uterus or ovaries surgically removed were excluded from the study. One hundred thirty-nine consecutive patients without abdominal or pelvic abnormality on sonography were selected. The local ethics committee approved the research project. Informed consent was obtained from every parent or guardian.

Pubertal development was classified according to Tanner puberty stages [11]. The presence of thelarche (onset of breast development) was the criterion used to distinguish pubertal girls from prepubertal girls. One hundred seventeen patients were classified as prepubertal (Tanner 1 for breast development; age range, 1–12 years; mean, 5.0 ± 2.7 years) and 22 as pubertal (Tanner score 2–4 for breast development; age range, 9–13 years; mean, 11.2 ± 1.2 years).

Sonography, in all patients, was performed and interpreted by the same physician. All patients underwent examinations with a full bladder, but a Foley catheter was not used. Although transvaginal sonography offers better image quality, it is not used in children because of the dimensions of the equipment. Sonography was thus performed using an SL 1 Ultrasonographer (Sono Line; Siemens, Erlangen, Germany) with 3.5- and 5-MHz transducers. Uterine measurements included the following: longitudinal diameter (*A*), transverse diameter (*B*), anteroposterior diameter (*C*), and diameter at the fundus divided by the diameter at the cervix (fundal–cervical ratio). Uterine volume was calculated in cubic centimeters using the ellipse formula $A \times B \times C \times 0.5233$. Uterine area was obtained in square centimeters by multiplying longitudinal diameter by transverse diameter ($A \times B$). Fundal–cervical ratio was measured to investigate the existence of a correlation between uterine morphology and thelarche (fundal–cervical ratio = 1 indicates prepubertal status; fundal–cervical ratio >1 indicates pubertal status).

TABLE 1 Uterine and Ovarian Volume According to Chronologic Age (n = 133)

Age (yr)	Uterine Volume (cm^3)				Ovarian Volume (cm^3)			
	No.	Mean	SD	Median	No.	Mean	SD	Median
1	8	0.91	0.40	0.91	3	0.26	0.12	0.24
2	14	1.30	0.68	1.10	10	0.38	0.11	0.38
3	18	1.26	0.44	1.22	13	0.37	0.11	0.32
4	14	1.48	0.79	1.35	14	0.46	0.14	0.47
5	10	1.81	0.44	1.77	10	0.52	0.22	0.49
6	14	1.84	1.09	2.03	12	0.65	0.23	0.70
7	12	2.27	1.23	2.41	11	0.59	0.25	0.47
8	8	2.07	1.38	1.55	8	0.69	0.30	0.65
9	7	3.43	1.08	2.97	6	0.93	0.23	0.95
10	6	3.50	2.70	2.50	5	1.15	0.18	0.70
11	12	4.63	2.70	3.85	11	1.12	0.43	1.21
12	7	10.92	5.27	9.94	7	1.88	1.56	1.37
13	3	16.15	10.78	14.56	3	2.94	1.30	3.03
Mean		2.87	3.68	1.75	113	0.77	0.73	0.56

The volume of each ovary was calculated using the same formula as that for calculation of uterine volume. Because the volumes of the right ovary (0.7 ± 0.8 cm^3) and left ovary (0.7 ± 0.7 cm^3) were not significantly different (Wilcoxon's test, p = 0.87), the final volume considered was the average volume for both ovaries [(right ovary volume + left ovary volume) / 2].

The morphologic appearance of the ovaries was also assessed. Because in most adults the average dimensions of a mature follicle range from 15 to 20 mm [12], completely cystic structures measuring up to 20 mm were classified as follicles, and larger structures were classified as cysts. To simplify and unify the varied nomenclature used to classify ovaries in terms of morphology, we used the following definitions: homogeneous ovaries, absence of cysts or visible follicles [13]; paucicystic ovaries, up to five follicles measuring less than 10 mm in diameter [8]; multicystic ovaries, more than six follicles mea-

suring less than 10 mm in diameter [8, 14]; macrocystic ovaries, one or more follicles measuring between 10 and 19 mm in diameter [4, 8, 15]; and ovaries presenting isolated cysts, one or more cysts measuring 20 mm or more in diameter [8].

After sonography, hand and wrist radiography was performed for the assessment of bone age. The radiologic tests of 73 girls were performed and interpreted by the same radiologist using the Greulich and Pyle scoring system [16]. Thirty-one radiographs (42%) were later reviewed by the same physician, with a good correlation ($r = 0.911$, $p < 0.0001$).

A significance level of p value less than or equal to 0.05 was used for the statistical analyses. Results were expressed as mean plus or minus standard deviation. For variables without a normal distribution, we used the following nonparametric tests: Wilcoxon's test for related samples, Mann-Whitney test for comparison between continuous variables in two groups, Kruskal-Wallis test for comparison among continuous variables in more than two groups, Fisher's exact test for comparison between categorical variables in two groups, and Spearman's correlation for testing ordinal variables. For variables with a normal distribution (bone age), the Pearson's correlation coefficient for testing continuous variables was used.

The curve estimation for uterine length, uterine area, and uterine and ovarian volume according to chronologic age was calculated using the linear, logarithmic, quadratic, cubic, and exponential models (8.0 for Windows; SPSS, Chicago, IL).

Results

The uterus was identified in 133 (96%) of 139 patients (age range, 1–13 years; mean, 6.1 ± 3.4 years). At least one ovary was visible in 129 girls (93%) (age range, 1–13 years; mean, 6.2 ± 3.4 years). Both ovaries were visualized in 113 girls (81%) (age range, 1–13 years; mean, 6.5 ± 3.3 years). In 10 girls, we were not able to visualize either ovary (age range, 1–7 years; mean, 2.5 ± 2.2 years).

The best curve estimation for uterine length, uterine area, and uterine and ovarian volume according to age was achieved with the cubic model. In the cubic equation $y = a + bx + cx^2 + dx^3$, y stands for uterine length, uterine area, uterine volume, or ovarian volume; x stands for age in years; and a, b, c, and d are constants calculated using the SPSS software for each of the variables. Therefore, we used the following equations:

$$\text{uterine length} = 2.2434 + 0.4479\ \text{age} - 0.0789\ \text{age}^2 + 0.0052\ \text{age}^3\ (r = 0.604;\ p < 0.0001);$$

$$\text{uterine area} = 0.7729 + 1.1011\ \text{age} - 0.2200\ \text{age}^2 + 0.0149\ \text{age}^3\ (r = 0.649;\ p < 0.0001);$$

$$\text{uterine volume} = -2.2671 + 2.7312\ \text{age} - 0.5558\ \text{age}^2 + 0.0345\ \text{age}^3\ (r = 0.629;\ p < 0.0001);$$

$$\text{ovarian volume} = -0.2408 + 0.4186\ \text{age} - 0.0754\ \text{age}^2 + 0.0046\ \text{age}^3\ (r = 0.500;\ p < 0.0001).$$

Uterine volume, area, and length and ovarian volume were smaller in patients without thelarche than in patients with thelarche (Mann-Whitney test, $p < 0.0001$): uterine volume was 1.8 ± 1.2 cm^3 versus 8.1 ± 6.6 cm^3 in patients without and with thelarche, respectively; uterine area was 2.7 ± 1.2 cm^2 versus 7.1 ± 3.3 cm^2; uterine length was 3.2 ± 0.7 cm versus 4.9 ± 1.1 cm; and ovarian volume was 0.5 ± 0.3 cm^3 versus 1.7 ± 1.2 cm^3. The group between 9 and 12 years old included pre- and postpubertal patients. In this age group, mean uterine length and ovarian volume were higher in patients with thelarche (Mann-Whitney test, $p < 0.03$) when compared with age-matched girls without thelarche.

Figures 1 and 2 show the increase in uterine and ovarian volume according to chronologic age and pubertal stage. Table 1 shows uterine and ovarian volume according to chronologic age. A progressive increase in these parameters can be observed with age. Figure 3 shows the distribution in percentiles 2.5, 50, and 97.5 of uterine length according to chronologic age. The patients with breast development are also identified in this figure. The cubic equation reveals different growth patterns for uterine area and length and uterine and ovarian volume. The mean ovarian and uterine size was smaller in girls up to 8 years, intermediate between 9 and 11 years, and larger after 11 years (Kruskal-Wallis test, $p < 0.0001$).

A statistically significant correlation occurred between chronologic age, bone age, and breast stage when compared with uterine length and area and uterine and ovarian volume, even in girls up to 7 years, as illustrated in Table 2. The association between sonographic variables and chronologic age is present both in the total sample ($n = 133$), in the prepubertal group (1–12 years old), and in patients up to 7 years old. Table 3 shows sonographic findings according to Tanner

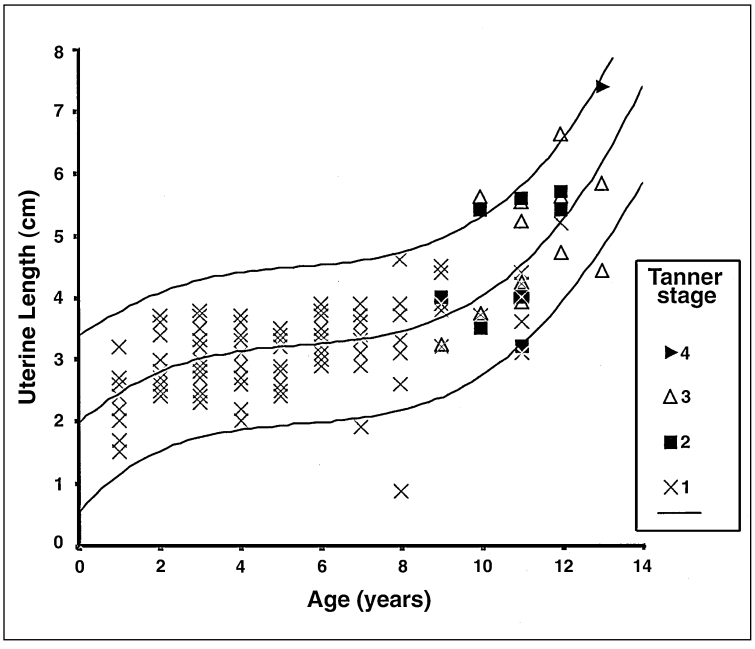

Fig. 3.—Scattergram shows distribution of uterine length according to age and Tanner stage. Lines represent percentiles 2.5, 50, and 97.5. Uterine length curve was best fitted by cubic model. Equation obtained with this mathematic model was uterine length = 2.2434 + 0.4479 age – 0.0789 age^2 + 0.0052 age^3 ($r = 0.604$, $p < 0.0001$).

stages [11]. All the sonographic variables that were assessed increased with the progression of pubertal development (Spearman's correlation, $p < 0.0001$).

In all patients without thelarche, the fundal–cervical ratio was equal to 1 ($n = 107$). However, in patients with thelarche, 12 (60%) had a fundal–cervical ratio equal to 1, and eight (40%) had a fundal–cervical ratio greater than 1. Thus, fundal–cervical ratio equal to 1 was specific (100%) to identify prepubertal girls but less specific to identify pubertal girls.

Eighteen of 139 ovarian follicles were observed in girls starting at 2 years old, as shown in Figure 4. Ovarian morphology was significantly different in patients with and without thelarche (Fisher's test, $p = 0.01$). A homogeneous pattern was found in 105 of 117 patients without thelarche and in 16 of 22 patients with thelarche. A paucicystic appearance was observed in 12 of 117 girls without thelarche and in four of 22 with thelarche. Multicystic ovaries were found in only two patients with thelarche (12 and 13 years old). Macrocysts and isolated cysts were not observed among the studied patients.

TABLE 2 Correlation of Uterine Length and Area and Uterine and Ovarian Volume with Chronologic Age, Bone Age, and Breast Stage in Patients Between 1 and 13 Years

Features	Pre- and Postpubertal (1–13 yr)	Prepubertal (1–12 yr)	Prepubertal (1–7 yr)	Bone Age (1–14 yr)	Breast Development Stage (1–4) (1–13 yr)
Correlation test	Spearman's $p < 0.0001$	Spearman's $p < 0.0001$	Spearman's $p < 0.0001$	Pearson's $p < 0.0001$	Spearman's $p < 0.0001$
Uterine length (cm)	$r = 0.680$ $n = 133$	$r = 0.525$ $n = 111$	$r = 0.429$ $n = 90$	$r = 0.650$ $n = 71$	$r = 0.536$ $n = 133$
Uterine area (cm^2)	$r = 0.669$ $n = 133$	$r = 0.492$ $n = 111$	$r = 0.381$ $n = 90$	$r = 0.692$ $n = 71$	$r = 0.555$ $n = 133$
Uterine volume (cm^3)	$r = 0.673$ $n = 133$	$r = 0.522$ $n = 111$	$r = 0.418$ $n = 90$	$r = 0.620$ $n = 71$	$r = 0.527$ $n = 133$
Ovarian volume (cm^3)	$r = 0.722$ $n = 113$	$r = 0.585$ $n = 92$	$r = 0.471$ $n = 73$	$r = 0.574$ $n = 61$	$r = 0.569$ $n = 113$

TABLE 3 Spearman's Correlation Between Pelvic Sonographic Parameters and Tanner Stage in Girls Between 1 and 13 Years Old

Features	Tanner Breast Stage			
	1	2	3	4
Uterine length (cm), $r = 0.536$, $p < 0.0001$				
No. measured	111	9	12	1
Mean	3.17[a,b]	4.72	4.87	7.40
SD	0.66	1.03	1.01	
Uterine area (cm^2), $r = 0.555$, $p < 0.0001$				
No. measured	111	9	12	1
Mean	2.74[a,b]	5.70[c]	7.40	15.54
SD	1.20	2.70	2.74	
Uterine volume (cm^3), $r = 0.52$, $p < 0.0001$				
No. measured	111	9	12	1
Mean	1.84[a,b]	5.48[c]	8.40	27.64
SD	1.23	5.01	4.89	
Mean ovarian volume (cm^3), $r = 0.569$, $p < 0.0001$				
No. measures	92	8	12	1
Mean	0.54[a,b]	1.09[c]	1.96	4.19
SD	0.25	0.43	1.31	

[a]Tanner stage 1 is different from stage 2 ($p < 0.05$).

[b]Tanner stage 1 is different from stage 3 ($p < 0.05$).

[c]Tanner stage 2 is different from stage 3 ($p < 0.05$).

Discussion

No consensus exists regarding standard values for uterine and ovarian measurements in healthy girls, although these standards are essential to identify pelvic disorders in this population [17].

In our study, a correlation was found between chronologic age, bone age, Tanner breast stage [11], and ovarian volume and uterine volume, area, and length, as also described in other studies [6, 8, 9, 18]. However, to our knowledge, our data are original in the sense that we show that this increase is also true for the group between 1 and 7 years old, which is the reference population in the study of patients with premature signs of puberty (isolated thelarche or central precocious puberty). In addition, the cubic equations calculated in our study can be used to predict uterine volume, length, and area, and ovarian volume in girls between 1 and 13 years. To our knowledge, there are no previous reports with these formulae.

Although some investigators [9, 10] argue that the ellipse formula is not the best method to calculate uterine volume because the uterus is not shaped like an ellipse—and, in fact, its shape changes over time—this is still the most common method used in sonographic studies [2, 4, 6, 17–21]. Therefore, we chose to use the ellipse formula in our study. However, as discussed by others [9, 10], future studies should pay more attention to uterine length, which, in this study, had a better correlation with age than uterine volume.

Bridges et al. [22] suggest that uterine shape, expressed as fundal–cervical ratio, is a better marker of pubertal development than other uterine dimensions. According to our results, the fundal–cervical ratio provided reliable information concerning pubertal status in girls up to 7 years old (fundal–cervical ratio = 1); however, after this age, the fundal–cervical ratio did not differentiate prepubertal and pubertal girls.

Some authors state that ovarian growth is influenced by age and by the onset of puberty [5, 23], whereas others state that it is influenced only by age [4, 17]. In our study, the difference in ovarian volume and uterine

length observed in 9- to 12-year-old patients with and without thelarche shows that both age and puberty affect uterine and ovarian size.

As previously described [24], there are two different stages of ovarian growth: the first one occurs at approximately 8 years old and results from adrenarche. The second stage occurs before the clinical manifestation of puberty and results from gonadotropin pulsatility. However, our results suggest that ovarian growth is influenced by age and by gonadarche.

Ovaries are dynamic organs that present both a stromal component, which increases discreetly from birth to maturity, and a gonadotropin-dependent follicular component [25]. Both the immature and the mature ovary have follicles in several stages of development or in atresia [26–30]. In addition, both types of follicles (atresic or not) may be cystic and can be observed from delivery until puberty on sonography [2, 4, 7, 10, 15, 17, 23, 27] or by histologic analyses [26, 27, 31]. This finding shows that follicular activity starts during intrauterine life [28]. During lactation and during the prepubertal and pubertal periods, higher levels of follicle-stimulating hormone are present [32]. Because microcysts are also frequently observed during these periods, we can postulate that the presence of ovarian follicles may be related to the increase in follicle-stimulating hormone levels.

In addition, we can postulate that the presence of microcysts at any age is physiologic, merely indicating the presence of anovulation and follicle-stimulating hormone stimulus. Thus, in infants or children, the usual ovarian pattern should be homogeneous or paucicystic. On the other hand, multicystic or macrocystic ovaries are usually associated with puberty or premature gonadal activity. Furthermore, in adolescents, ovarian volume and hyperechogenic stroma, rather than the isolated findings of microcysts, seem to be an important variable to differentiate multicystic from polycystic ovaries [33].

In our study, we used a simplified classification of ovarian morphology because the current classifications are not standardized, and their application in clinical practice is compromised by the variations in nomenclature. Therefore, we believe that a simplification in this terminology can be useful for clinicians. According to our classification, homogeneous ovaries were more frequent in patients without thelarche, and multicystic ovaries, in patients with thelarche. No differences were found in the frequency of paucicystic ovaries in patients with or without thelarche. Buzi et al. [8] reported similar findings.

In conclusion, the growth of the uterus and ovaries is proportional to chronologic age, bone age, and pubertal stage. Even in prepubertal girls, age influenced sonographic variables. The mean rate of uterine and ovarian growth was slower until 8 years old, intermediate between 9 and 11 years old, and higher after this age because of the progression of puberty.

The presence of some ovarian follicles is nonspecific and physiologic in infants, children, and adolescents. However, the presence of six or more follicles (multicystic ovaries) seems to be correlated with pubertal stimuli both in normal and precocious puberty.

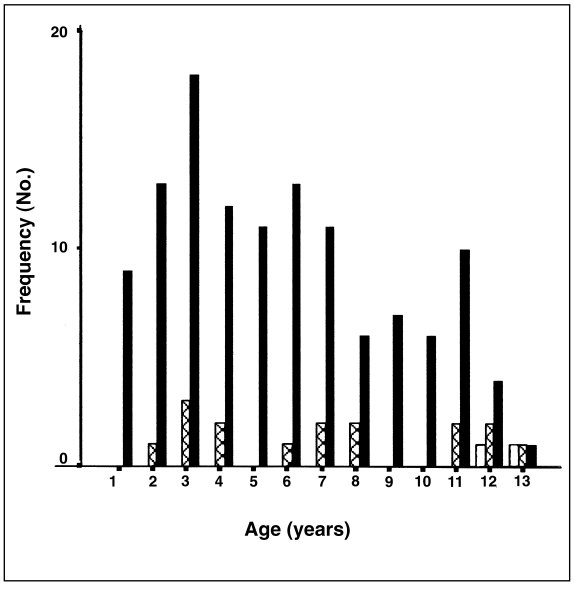

Fig. 4.—Bar chart shows ovarian morphology versus age. Homogeneous (black bar) = absence of visible follicles, paucicystic (checkered bar) = up to five follicles measuring less than 10 mm in diameter, multicystic (white bar) = six or more follicles measuring less than 10 mm in diameter.

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