Anti-Müllerian Hormone in Girls with Premature Adrenarche: The Impact of Polycystic Ovary Syndrome History in their Mothers

Alexandra Efthymiadou, MD, PhD, Maria Bogiatzidou, MD, Dimitra Kritikou, PhD, and Dionisios Chrysis, MD, PhD

Objectives To assess whether the serum levels of anti-Müllerian hormone (AMH) are increased in girls with premature adrenarche because they are at a higher risk of developing polycystic ovary syndrome (PCOS) later in life.
Study design We measured serum levels of AMH, dehydroepiandrosterone sulfate (DHEAS), testosterone, sex hormone binding globulin, androstenedione, and 17-hyroxyprogesterone in 89 girls with premature adrenarche aged 6.98 ± 1.60 years, and in 55 prepubertal normal girls aged 6.78 ± 1.60 years.
Results AMH was significantly higher in girls with premature adrenarche (2.95 ± 1.20 ng/mL) compared with normal prepubertal girls (2.00 ± 0.95 ng/mL; $P < .001$), whereas their body mass index SD score was similar ($P > .05$). DHEAS, testosterone, and androstenedione were increased in premature adrenarche, whereas sex hormone binding globulin was decreased in girls with premature adrenarche. Among the 89 girls with premature adrenarche, 33 were daughters of mothers with a positive history of PCOS, whereas the mothers of the remaining 56 girls with premature adrenarche had a negative history of PCOS. The girls with a mother with a positive history of PCOS had significantly higher AMH serum levels compared with girls with a mother with a negative history of PCOS (3.37 ± 1.72 ng/mL vs 2.70 ± 1.25 ng/mL; $P < .05$) with no differences in testosterone, DHEAS, androstenedione, and sex hormone binding globulin. The serum concentration of AMH was only positively related to androstenedione ($r = 0.538$; $P < .0001$).
Conclusions Girls with premature adrenarche, especially those from mothers with a history of PCOS, could have a higher risk of developing PCOS later in life because they have increased serum AMH. *(J Pediatr 2019;205:190-4).*

Premature adrenarche has been considered as a benign condition when excluding pathologic causes of hyperandrogenism, such as adrenal tumors and nonclassical adrenal hyperplasia. However, premature adrenarche has been associated with an increased risk of functional hyperandrogenism and hyperinsulinism in adolescence and increased risk for the development of polycystic ovarian syndrome (PCOS), especially in those born small for gestational age.[1]

Anti-Müllerian hormone (AMH) in females is produced by the granulosa cells in the ovaries.[2] During postnatal life, AMH serum levels are lower in females than in males, but they increase around 6-8 years of age, reach a peak during late adolescence, and thereafter decline along their reproductive life.[3] There is a good correlation between AMH serum levels and preantral and small antral follicular reserve in reproductive aged women.[4] In women and adolescents with PCOS, AMH serum levels are increased compared with healthy females[5,6] and reflect the severity of PCOS.[7] Furthermore, studies have proposed the measurement of AMH serum levels as a diagnostic test for PCOS.[7,8]

Because girls with premature adrenarche could have a higher risk of developing PCOS in adolescence and AMH is increased in adolescent girls and adult women with PCOS, we hypothesized that serum AMH would be increased, even in prepubertal girls with premature adrenarche. The available data are inconclusive because increased,[9] decreased,[10] or even unchanged[11] serum AMH levels have been reported in girls with premature adrenarche. Additionally, studies have demonstrated that PCOS is more frequent in first-degree relatives[12,13] and prepubertal and peripubertal daughters of women with PCOS have higher serum AMH levels compared with control girls.[14,15] Therefore, we investigated whether the AMH serum concentration is altered in girls with premature adrenarche and if the presence of PCOS history in their mothers has an additional effect.

Methods

A total of 89 girls with premature adrenarche and 55 healthy control girls were enrolled in the study. The clinical inclusion criteria for premature adrenarche were the onset of signs of adrenarche before the age of 8 years and the presence of pubic or axillary hair. Patients with clitoris

BMI	Body mass index
DHEAS	Dehydroepiandrosterone sulfate
PAN	Negative history of PCOS
PAP	Positive history of PCOS
PCOS	Polycystic ovarian syndrome
SHBG	Sex hormone binding globulin

From the Division of Endocrinology Department of Pediatrics, Medical School, University of Patras, Patra, Greece

Supported by the Research Committee of the University of Patras (Grant ID: B435).

The authors declare no conflicts of interest.

https://doi.org10.1016/j.jpeds.2018.09.064

enlargement and pubertal girls were excluded. All girls were followed for ≥6 months and none entered puberty. None of the patients or control subjects were on any medication. Birth weight and length were recorded from the national book of child's health and we included only girls born appropriate for gestational age. Detailed information was obtained from the mothers for the presence of history of PCOS, menstrual irregularities, and hirsutism. Mothers with PCOS were defined as only those diagnosed by an endocrinologist or gynecologist ≥2 years after menarche. Daughters of women with PCOS were excluded from the control group. Daughters of women with no defined diagnosis of PCOS but with a history of menstrual irregularities or hirsutism were also excluded from the study. The control group consisted of girls attending our community pediatric outpatient clinic for routine health visits and blood screening, or our paediatric department for preoperative assessment for minor surgeries. Age, height (measured by a Harpenden stadiometer), and weight were measured, and pubertal status was clinically assessed according to Tanner stages. Height, weight, and body mass index (BMI) were expressed as the SDS of the Greek reference data, which were automatically calculated by the software program Growth Analyzer 3 (Dutch Growth Research Foundation, Rotterdam, The Netherlands). Bone age from girls with premature adrenarche was assessed by the same senior pediatric endocrinologist based on radiographs from the left hand and wrist evaluated according to Greulich and Pyle atlas. The study was approved by the Ethics Committee of the University Hospital of Patras. All children and their parents were informed, and written consent was obtained before participation in the study.

Methods

Blood was collected at 8:00 a.m. after overnight fasting for the assessment of AMH, sex hormone binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEAS), testosterone, androstenedione, and 17OH progesterone. An adrenocorticotrophic hormone stimulation test was performed in cases with baseline 17OH progesterone of >2 ng/mL to exclude late-onset congenital adrenal hyperplasia owing to 21 hydroxylase deficiency. Patients with late-onset congenital adrenal hyperplasia were excluded from the study.

Serum DHEAS, SHBG, and testosterone were measured by chemiluminescence assay (Roche Elecsys, Roche Diagnostics, Athens, Greece), AMH by 2-site ELISA (Diagnostic System Laboratories, Webster, Texas), androstenedione and 17OH progesterone by radioimmunoassay.

Statistical Analyses

Statistical analysis was performed with SPSS 20 software for Windows (SPSS, Inc, Chicago, Illinois). Data were expressed as mean ± SD for parametric or median (range) for nonparametric data distribution. Differences between groups were analyzed by using the Student *t* test for parametric and the Mann-Whitney *U* test for nonparametric data distribution (DHEAS, testosterone, and 17OH progesterone) for comparison between controls and girls with premature adrenarche, or 1-way ANOVAs with the Newman-Keuls multiple comparison test for parametric data and the Kruskal-Wallis test with the Dunn multiple comparison test for nonparametric data. For univariate analysis, the Pearson correlation test was used for parametric data distribution and the Spearman correlation for nonparametric data distribution. Partial correlations were performed with adjustment as appropriate for various parameters affecting the variables compared (age and BMI). Any *P* value of <.05 were considered as statistically significant.

Results

Controls and girls with premature adrenarche had similar age and BMI SDS, but girls with premature adrenarche were taller ($P < .0001$) and had higher AMH ($P < .001$), DHEAS ($P < .0001$), testosterone ($P < .0001$), and androstenedione serum levels ($P < .0001$) (**Table I**). In contrast, SHBG serum concentration was decreased in the premature adrenarche compared with control girls ($P < .001$), but 17OH progesterone serum concentration was similar in the 2 groups. Bone age was advanced by 0.49 years in girls with premature adrenarche (**Table I**).

Age was positively related with androstenedione ($r = 0.26$; $P < .01$), DHEAS ($r = 0.32$; $P < .001$), and testosterone ($r = 0.33$; $P < .001$), and negatively with SHBG ($r = -0.17$; $P < .05$). BMI SDS was positively related to DHEAS ($r = 0.23$; $P < .01$) and androstenedione ($r = 0.23$; $P < .01$), and negatively with SHBG ($r = -0.35$; $P < .001$). BMI SDS was negatively related to AMH only in the control group ($r = -0.15$; $P < .05$).

After partial adjustment for age and BMI, AMH was positively related to androstenedione ($r = 0.538$; $P < .0001$) (**Figure 1**), and DHEAS was positively related to androstenedione ($r = 0.31$; $P < .001$) and testosterone ($r = 0.41$, $P < .0001$) and negatively to SHBG ($r = -0.24$, $P < .01$). Androstenedione was positively related to testosterone ($r = 0.18$; $P < .05$) and negatively to SHBG ($r = -0.26$; $P < .01$); testosterone was nega-

Table I. Anthropomorphic and hormonal data in controls and girls with premature adrenarche

	Controls	Girls with premature adrenarche
N	55	89
Age, y	6.78 ± 1.60	6.98 ± 1.60
Bone age, y		7.47 ± 1.62
BMI SDS	1.02 ± 1.60	1.26 ± 1.02
Height SDS	−0.69 ± 1.30	0.288 ± 1.00*
AMH, ng/mL	2.00 ± 0.95	2.95 ± 1.20†
DHEAS, μg/dL	23.26 (0.99-139.00)	90.40 (30.00-279.00)*
Testosterone, ng/dL	2.90 (2.00-8.00)	6.40 (2.00-57.20)*
Androstenedione, ng/mL	0.27 ± 0.13	0.99 ± 0.47*
SHBG, nmol/L	102.60 ± 42.00	81.16 ± 30.77†
17OH progesterone, ng/mL	0.40 (0.10-3.10)	0.70 (0.10-4.50)

All data are expressed as mean ± SD (parametric data distribution) except for DHEAS, testosterone, and 17OH progesterone, which are median (range) (nonparametric data distribution). For comparison of mean values of variables between girls with premature adrenarche and control girls, an unpaired Student *t* test was used, and for nonparametric data, median values were compared with the Mann-Whitney *U* test.
*$P < .001$.
†$P < .0001$.

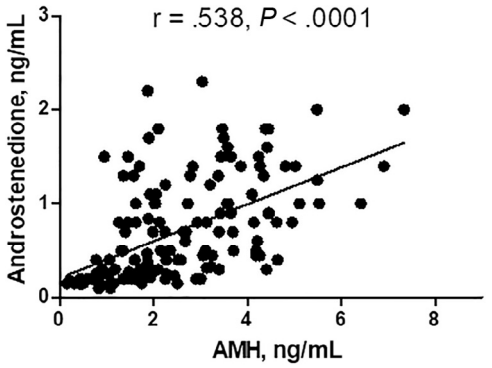

Figure 1. Correlation of AMH and androstenetione serum levels was studied after adjustment for age and BMI.

tively related to SHBG (r = −0.22; $P < .05$), whereas 17OH progesterone was positively related to androstenedione (r = 0.27; $P < .05$).

Then, girls with premature adrenarche were divided into 2 groups according to the presence of a history of PCOS in their mothers: girls with premature adrenarche from mothers with a negative history of PCOS (PAN) and girls with premature adrenarche from mothers with a positive history of PCOS (PAP). The control, PAN, and PAP groups had similar ages and BMI. Bone age was slightly more advanced in the PAP group compared with the PAN group ($P < .05$), but they had similar height, and both were taller than the control group (**Table II**).

AMH serum levels were significantly increased in both the PAN and PAP groups compared with the control group ($P < .001$ and $P < .01$, respectively), whereas the PAP group had substantially higher AMH levels than the PAN group ($P < .05$) (**Table II** and **Figure 2**, B). The rest of the examined biochemical indices (DHEAS, testosterone, androstenedione, SHBG, and 17OH progesterone) were increased in the PAN and PAP groups compared with the control group, but were similar in both groups with premature adrenarche (**Table II**).

Discussion

In the present study, we found that AMH concentration is increased in girls with premature adrenarche compared with healthy girls and that the presence of a history of PCOS in their mothers enhances it further. Girls within the PAP group had more advanced bone age compared with girls in the PAN group, but all the other assessed hormonal indices did not differ significantly.

Data on AMH serum levels in girls with premature adrenarche are limited to 3 studies with contradictory results. The differences between our results and those reported by Utriainen et al[10] and Ucar et al[11] could most likely be explained by differences in age, ethnic background, and selection criteria. Furthermore, our results are not influenced by the BMI as reported by Utriainen et al[10] in girls with premature adrenarche because we matched the 2 groups to have similar BMI SDS. There is some controversy as to whether AMH levels are affected by BMI in normal women, women with PCOS,[16-18] and prepubertal girls.[10]

Although premature adrenarche has been considered a benign condition, recent data in literature have shown that it could be associated with insulin resistance, increased cardiovascular risk (the metabolic syndrome), ovarian hyperandrogenism, and an increased risk for PCOS,[1,19,20] especially in those girls with premature adrenarche and a low birth weight. However, not all girls with premature adrenarche will be at risk of developing the conditions mentioned herein, and other studies have failed to find a link between premature adrenarche and low birth weight, insulin resistance, or ovarian hyperandrogenism.[21,22] Because low birth weight has been linked to altered gonadal function and PCOS[23,24] and with increased AMH concentration even in early infancy,[25] we recruited only girls born appropriate for gestational age to eliminate the possible influence of low birth weight on AMH serum levels.

The increased AMH serum concentration we found in girls with premature adrenarche does not directly show an increased risk of developing PCOS later in life but, at least from the available data in the literature, suggests an increased ovarian follicular pool and altered follicular development. Whereas there are controversies whether girls with premature adrenarche are at a higher risk of developing PCOS, studies have shown that daughters of women with PCOS have more often exaggerated adrenarche,[26] suggesting that a link could exist between premature adrenarche and PCOS. In contrast, women with PCOS have increased AMH serum levels, as well as their daughters in infancy, in childhood but also in puberty with increased ovarian volume[14,15,27] in the absence of premature adrenarche, suggesting altered follicular development, a feature associated with PCOS. These studies indicate that PCOS-related alterations could even start before puberty. Indeed, the daughters of women with PCOS more often develop PCOS compared with the general population, supporting the hypothesis that the elevated AMH levels in these girls could be an early marker of higher risk. Our study is in agreement with findings that show increased AMH levels in prepubertal daughters of women with PCOS without adrenarche[14] because our PAP group had elevated serum AMH levels compared not only with the control, but also to the PAN group. The increased AMH levels in our girls with premature adrenarche could indicate that as a group they have increased follicular development and may be at higher risk of developing PCOS later in life. Longitudinal studies are needed to clarify whether the girls with premature adrenarche with increased AMH concentration will more frequently develop PCOS later in life compared with the general population. We acknowledge here, as a limitation of our study, that the definition of mothers with PCOS was based on self-reporting. Because we cannot rule out some false-positive inclusions, the increased AMH is most likely underestimated since the premature adrenarche with a PAN in their mothers had lower levels of AMH.

Table II. Anthropomorphic and hormonal data in controls and with girls with premature adrenarche in the PAN and PAP groups

	Controls	PAN	PAP
N	55	56	33
Age, y	6.78 ± 1.60	6.97 ± 1.30	7.04 ± 1.10
Bone age, y	—	7.22 ± 1.81*	7.85 ± 1.24
BMI SDS	1.02 ± 1.60	1.32 ± 1.10	1.15 ± 0.90
Height SDS	–0.69 ± 1.30	0.14 ± 1.04†	0.52 ± 0.91†
AMH, ng/mL	2.00 ± 0.95	2.70 ± 1.25‡,*	3.37 ± 1.72†
DHEAS, μg/dL	23.26 (0.99-139.00)	97.60 (30.00-261.00)†	80.00 (38.00-279.00)†
Testosterone, ng/mL	2.90 (2.00-8.00)	7.27 (2.00-57.20)†	5.60 (9.00-40.00)‡
Androstenedione, ng/mL	0.27 ± 0.13	0.94 ± 0.45§	1.07 ± 0.50§
SHBG nmol/L	102.60 ± 42.00	82.84 ± 33.51¶	78.30 ± 25.71‡
17OH progesterone, ng/mL	0.40 (0.10-3.10)	0.75 (0.20-4.50)	0.6 (0.10-3.70)

All data are expressed as mean ± SD (parametric data distribution) except for DHEAS, testosterone, and 17OH progesterone, which are median (range) (nonparametric data distribution). For comparison of mean values of variables between control, PAN, and PAP girls 1-way ANOVA with the Newman-Keuls multiple comparison test for parametric data was used, and for nonparametric data the Kruskal-Wallis statistic with Dunn multiple comparison test was used. Median values of 17OH progesterone were compared with the Mann-Whitney *U* test in the 2 premature adrenarche groups.
*$P < .05$ vs PAP.
†$P < .01$ vs control.
‡$P < .001$ vs control.
§$P < .0001$ vs control.
¶$P < .05$ vs control.

The mechanisms behind the increased AMH in premature adrenarche are not known. Most of the data in the literature on the regulation of AMH are derived from postpubertal women or animals; therefore, it is difficult to extrapolate to prepubertal girls. The increased androgens without the presence of estrogens in the prepubertal girls with premature adrenarche could be a possible mechanism, because the upregulation of AMH messenger RNA has been reported by androgens in small follicles from women with PCOS.[28] The positive correlation between androstenedione and AMH is a supportive indication that as it has been reported in adult women with PCOS.[29] More factors are involved because PAN and PAP groups have similar androgen levels, but different AMH concentrations. The positive family history of PCOS in girls with PAP shows that the genetic background could be one of those factors, which are also reported in the daughters of women with PCOS without adrenarche.[14,15]

PCOS does not exist in prepubertal girls; in adolescent girls, the diagnosis is challenging because the normal physiology of puberty often presents with features similar to those of PCOS. Therefore, a biochemical marker indicating a higher risk of PCOS would be valuable in situations associated with PCOS later in life. AMH is a possible candidate because it is increased in PCOS, reflecting the increased number of growing follicles,[30,31] correlates with the severity of PCOS,[32] and has been proposed as a useful marker in the diagnosis of women with PCOS.[7,8] In our study, although the girls with premature adrenarche as a group had elevated AMH serum levels, the overlapping of the AMH values was broad; therefore, it cannot be a useful marker identifying those girls with premature adrenarche who have a higher risk of developing PCOS later in life. In contrast, in girls with premature adrenarche, the presence of PCOS history in their mothers may further increase the risk of PCOS because AMH is even higher compared with girls with premature adrenarche with no history of PCOS in their mothers. Knowing that hyperandrogenic symptoms and polycystic ovaries are more frequent in the first-degree relatives of patients with PCOS compared with controls,[12,13,33] the

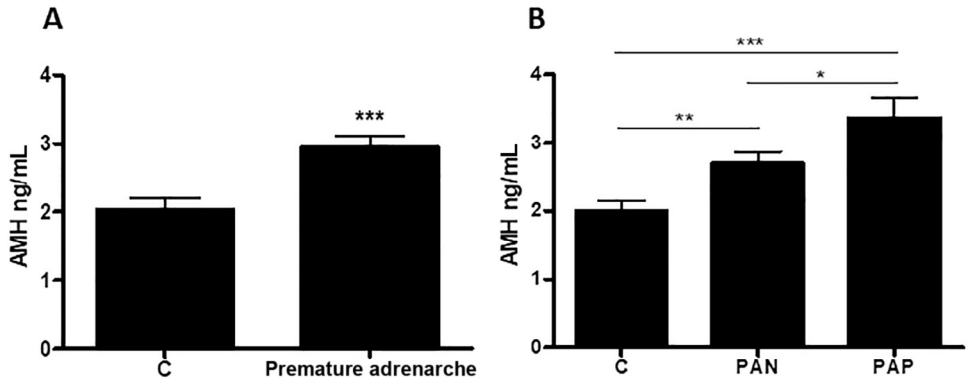

Figure 2. **A,** AMH serum levels in control (C) and with girls with premature adrenarche. **B,** AMH serum levels in C and in girls with premature adrenarche in the PAN and PAP groups. *$P < .05$, **$P < .001$, ***$P < .001$.

elevated serum AMH levels in the daughters of women with PCOS with or without premature adrenarche may suggest a possible risk of developing PCOS later in life. Longitudinal studies are needed to clarify the possible relationship of premature adrenarche with the development of PCOS in late adolescence. ■

Submitted for publication Jun 5, 2018; last revision received Aug 14, 2018; accepted Sep 26, 2018

Reprint requests: Dionisios Chrysis, MD, PhD, Division of Endocrinology, Department of Pediatrics, Medical School, University of Patras, Rion Patra, 26500, Greece. E-mail: dchrysis@upatras.gr

References

1. Ibanez L, Dimartino-Nardi J, Potau N, Saenger P. Premature adrenarche—normal variant or forerunner of adult disease? Endocr Rev 2000;21:671-96.
2. Lee MM, Donahoe PK. Mullerian inhibiting substance: a gonadal hormone with multiple functions. Endocr Rev 1993;14:152-64.
3. Lee MM, Donahoe PK, Hasegawa T, Silverman B, Crist GB, Best S, et al. Mullerian inhibiting substance in humans: normal levels from infancy to adulthood. J Clin Endocrinol Metab 1996;81:571-6.
4. Grynnerup AG, Lindhard A, Sorensen S. The role of anti-Mullerian hormone in female fertility and infertility—an overview. Acta Obstet Gynecol Scand 2012;91:1252-60.
5. Nardo LG, Yates AP, Roberts SA, Pemberton P, Laing I. The relationships between AMH, androgens, insulin resistance and basal ovarian follicular status in non-obese subfertile women with and without polycystic ovary syndrome. Hum Reprod 2009;24:2917-23.
6. Siow Y, Kives S, Hertweck P, Perlman S, Fallat ME. Serum Mullerian-inhibiting substance levels in adolescent girls with normal menstrual cycles or with polycystic ovary syndrome. Fertil Steril 2005;84:938-44.
7. Jacob SL, Field HP, Calder N, Picton HM, Balen AH, Barth JH. Anti-Mullerian hormone reflects the severity of polycystic ovary syndrome. Clin Endocrinol (Oxf) 2016;86:395-400.
8. Iliodromiti S, Kelsey TW, Anderson RA, Nelson SM. Can anti-Mullerian hormone predict the diagnosis of polycystic ovary syndrome? A systematic review and meta-analysis of extracted data. J Clin Endocrinol Metab 2013;98:3332-40.
9. Paterson WF, Ahmed SF, Bath L, Donaldson MD, Fleming R, Greene SA, et al. Exaggerated adrenarche in a cohort of Scottish children: clinical features and biochemistry. Clin Endocrinol (Oxf) 2010;72:496-501.
10. Utriainen P, Jaaskelainen J, Voutilainen R. Serum anti-Mullerian hormone concentrations in prepubertal girls with and without premature adrenarche: the influence of body mass index. Horm Res Paediatr 2010;74:207-11.
11. Ucar A, Erol OB, Yekeler E, Yildiz I, Bozlak S, Saka N, et al. Pelvic ultrasound findings in prepubertal girls with precocious adrenarche born appropriate for gestational age. Clin Endocrinol (Oxf) 2014;80:699-705.
12. Govind A, Obhrai MS, Clayton RN. Polycystic ovaries are inherited as an autosomal dominant trait: analysis of 29 polycystic ovary syndrome and 10 control families. J Clin Endocrinol Metab 1999;84:38-43.
13. Lunde O, Magnus P, Sandvik L, Hoglo S. Familial clustering in the polycystic ovarian syndrome. Gynecol Obstet Invest 1989;28:23-30.
14. Sir-Petermann T, Codner E, Maliqueo M, Echiburu B, Hitschfeld C, Crisosto N, et al. Increased anti-Mullerian hormone serum concentrations in prepubertal daughters of women with polycystic ovary syndrome. J Clin Endocrinol Metab 2006;91:3105-9.
15. Crisosto N, Codner E, Maliqueo M, Echiburu B, Sanchez F, Cassorla F, et al. Anti-Mullerian hormone levels in peripubertal daughters of women with polycystic ovary syndrome. J Clin Endocrinol Metab 2007;92:2739-43.
16. Freeman EW, Gracia CR, Sammel MD, Lin H, Lim LC, Strauss JF 3rd. Association of anti-mullerian hormone levels with obesity in late reproductive-age women. Fertil Steril 2007;87:101-6.
17. Skalba P, Cygal A, Madej P, Dabkowska-Huc A, Sikora J, Martirosian G, et al. Is the plasma anti-Mullerian hormone (AMH) level associated with body weight and metabolic, and hormonal disturbances in women with and without polycystic ovary syndrome? Eur J Obstet Gynecol Reprod Biol 2011;158:254-9.
18. Kriseman M, Mills C, Kovanci E, Sangi-Haghpeykar H, Gibbons W. Antimullerian hormone levels are inversely associated with body mass index (BMI) in women with polycystic ovary syndrome. J Assist Reprod Genet 2015;32:1313-6.
19. Williams RM, Ward CE, Hughes IA. Premature adrenarche. Arch Dis Child 2012;97:250-4.
20. Ibanez L, Diaz R, Lopez-Bermejo A, Marcos MV. Clinical spectrum of premature pubarche: links to metabolic syndrome and ovarian hyperandrogenism. Rev Endocr Metab Disord 2009;10:63-76.
21. Utriainen P, Laakso S, Liimatta J, Jaaskelainen J, Voutilainen R. Premature adrenarche—a common condition with variable presentation. Horm Res Paediatr 2015;83:221-31.
22. Idkowiak J, Lavery GG, Dhir V, Barrett TG, Stewart PM, Krone N, et al. Premature adrenarche: novel lessons from early onset androgen excess. Eur J Endocrinol 2011;165:189-207.
23. Ibanez L, Potau N, Francois I, de Zegher F. Precocious pubarche, hyperinsulinism, and ovarian hyperandrogenism in girls: relation to reduced fetal growth. J Clin Endocrinol Metab 1998;83:3558-62.
24. Cresswell JL, Barker DJ, Osmond C, Egger P, Phillips DI, Fraser RB. Fetal growth, length of gestation, and polycystic ovaries in adult life. Lancet 1997;350:1131-5.
25. Sir-Petermann T, Marquez L, Carcamo M, Hitschfeld C, Codner E, Maliqueo M, et al. Effects of birth weight on anti-mullerian hormone serum concentrations in infant girls. J Clin Endocrinol Metab 2010;95:903-10.
26. Maliqueo M, Sir-Petermann T, Perez V, Echiburu B, de Guevara AL, Galvez C, et al. Adrenal function during childhood and puberty in daughters of women with polycystic ovary syndrome. J Clin Endocrinol Metab 2009;94:3282-8.
27. Sir-Petermann T, Ladron de Guevara A, Codner E, Preisler J, Crisosto N, Echiburu B, et al. Relationship between anti-Mullerian hormone (AMH) and insulin levels during different tanner stages in daughters of women with polycystic ovary syndrome. Reprod Sci 2012;19:383-90.
28. Pierre A, Taieb J, Giton F, Grynberg M, Touleimat S, El Hachem H, et al. Dysregulation of the anti-Mullerian hormone system by steroids in women with polycystic ovary syndrome. J Clin Endocrinol Metab 2017;102:3970-8.
29. Piltonen T, Morin-Papunen L, Koivunen R, Perheentupa A, Ruokonen A, Tapanainen JS. Serum anti-Mullerian hormone levels remain high until late reproductive age and decrease during metformin therapy in women with polycystic ovary syndrome. Hum Reprod 2005;20:1820-6.
30. Pigny P, Merlen E, Robert Y, Cortet-Rudelli C, Decanter C, Jonard S, et al. Elevated serum level of anti-mullerian hormone in patients with polycystic ovary syndrome: relationship to the ovarian follicle excess and to the follicular arrest. J Clin Endocrinol Metab 2003;88:5957-62.
31. Laven JS, Mulders AG, Visser JA, Themmen AP, De Jong FH, Fauser BC. Anti-Mullerian hormone serum concentrations in normoovulatory and anovulatory women of reproductive age. J Clin Endocrinol Metab 2004;89:318-23.
32. Piouka A, Farmakiotis D, Katsikis I, Macut D, Gerou S, Panidis D. Anti-Mullerian hormone levels reflect severity of PCOS but are negatively influenced by obesity: relationship with increased luteinizing hormone levels. Am J Physiol Endocrinol Metab 2009;296:E238-43.
33. Hague WM, Adams J, Reeders ST, Peto TE, Jacobs HS. Familial polycystic ovaries: a genetic disease? Clin Endocrinol (Oxf) 1988;29:593-605.