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Elevated Serum Anti-Müllerian Hormone in Adolescents with Polycystic Ovary Syndrome: Relationship to Ultrasound Features

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Abstract

Context—Serum Anti-Müllerian Hormone (AMH) is linked to the ovarian follicle pool. Little is known about the relationship between serum AMH and ovarian ultrasound (US) features in adolescents with Polycystic Ovary Syndrome (PCOS).

Objectives—To confirm that serum AMH is elevated in adolescents with PCOS and to correlate serum AMH with ovarian ultrasound features in this population.

Design—A retrospective chart review of clinical, biochemical, and ultrasonographic data in adolescents with PCOS and normal controls. Serum AMH was measured and compared between groups and correlated with ovarian ultrasound findings.

Setting—Two urban tertiary academic medical centers.

Participants—Study groups included 23 adolescent females with PCOS and 12 age and BMI matched female controls.

Main Outcome Measures—We hypothesized that serum AMH would be elevated in the PCOS group compared with controls and would positively correlate with follicle number, distribution, and ovarian volume.

Results—Serum AMH was 6.78 +−3.55 ng/mL in the PCOS group versus 3.38 +−1.48 ng/mL in controls (P=0.0004). AMH positively correlated with ovarian volume (left ovary r=0.65, P=0.0007, right ovary r=0.55, P=0.0065) and peripheral follicle distribution (P=0.0027). Ten or more follicles were observed in 83% of ultrasounds.

Conclusions—There is a positive relationship between serum AMH and ovarian volume as well as peripheral follicular distribution in adolescents with PCOS. Our findings support the use of serum AMH as a useful marker to reflect ovarian ultrasound features typical of PCOS in cases where accurate ultrasounds are not available and for follow up.

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Keywords

Polycystic Ovary Syndrome; Anti-Müllerian Hormone; Adolescents

Introduction

Polycystic Ovary Syndrome (PCOS) is the one of the most prevalent endocrine-metabolic disorders afflicting females of reproductive age (1,2). Although the pathophysiology associated with PCOS may begin prior to menarche, the disorder often initially manifests in adolescence. Diagnosing PCOS in adolescents can be challenging as irregular menses is common following menarche, adolescents frequently suffer from acne, and hirsutism may be significantly less prevalent in this age group (3). Therefore, the Rotterdam ultrasonographic criteria (4) may lend particular credence to PCOS diagnosis in this population. Unfortunately, obtaining optimal ultrasounds is often impaired by the inability to perform transvaginal ultrasounds in adolescents. Obesity often prevents the attainment of high quality transabdominal ultrasounds. A marker that correlates with the ovarian ultrasonographic features seen in PCOS would therefore be a particularly useful adjunct to assist in the diagnosis and/or follow up of PCOS in adolescents.

Anti-Müllerian Hormone (AMH) is a 140 k-Da dimeric glycoprotein member of the TGF-β superfamily. Perhaps best known for its role in Müllerian duct regression in males (5,6), AMH is also produced by ovarian granulosa cells in preantral and antral follicles starting at 36 weeks gestation until menopause. (7–11). PCOS is characterized by an increase in preantral and antral follicle number. Serum AMH levels are 2–3 times higher in adult women with PCOS compared with healthy controls and positively correlate with antral follicle count (12–14). Studies have demonstrated elevated serum AMH levels in adolescents with PCOS and in peripubertal daughters of women with PCOS (15–17). In this study, we sought to determine whether AMH is a useful biomarker for ovarian ultrasound characteristics in adolescent PCOS by correlating serum AMH with follicular number, distribution, and ovarian volume. In addition, we aimed to confirm the elevation of serum AMH in adolescents with PCOS compared with obese controls and relate serum AMH to markers of insulin resistance and hyperandrogenism.

Subjects and Methods

Patient Population

The Institutional Review Board of New York University School of Medicine and Bellevue Hospital approved this cross-sectional retrospective study. Data was reviewed from 2005–2010. All patients were followed by the Pediatric Endocrinology service at Bellevue Hospital Center or New York University Medical Center, two large urban academic tertiary care centers. We studied 23 females (age 12.3–17.7 years) with PCOS and 12 age, BMI, and sex matched controls (age 11.4–16.5 years). Table 1 shows all subjects baseline demographic and clinical characteristics obtained from a chart review. Exclusion criteria included pregnancy, ovarian or androgen secreting tumor, thyroid dysfunction, hyperprolactinemia, Cushing syndrome, and congenital adrenal hyperplasia. No subject was taking insulin sensitizers or any medication known to influence the menstrual cycle. The diagnosis of PCOS was based on the revised 2003 ESHRE/ASRM Rotterdam criteria (3), which require two out of three following characteristics: (1) oligo/anovulation, (2) clinical/biochemical signs of hyperandrogenism, and (3) polycystic ovaries on ultrasound (the presence of 12 or more follicles measuring 2–9 mm in diameter and/or ovarian volume > 10 ml). Hirsutism was defined as a Ferriman-Gallwey grade of 8 or higher. Amenorrhea was defined as cessation of periods for more than 3 months. Oligomenorrhea was defined as less

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than 6 cycles per year. Only post-menarcheal subjects were selected. Based on data from the National Health and Nutrition Examination Survey, overweight was defined as a BMI between the 85–95th % and obese as a BMI > 95th% for age and sex.

Hormonal Immunoassays

Blood samples from the PCOS group and controls were obtained during routine Pediatric Endocrinology clinic visits. Blood sample collection was not timed with respect to menstrual cycle. Total Testosterone was measured by well validated LC/MS with an analytical sensitivity of 1 ng/dL (Quest Diagnostics). The percent free Testosterone was determined by equilibrium dialysis. The free Testosterone level was calculated based on total and percent free. Biochemical hyperandrogenism was defined as a free Testosterone of 7.5 pg/mL or greater. Fasting serum insulin was determined by radioimmunoassay with a lower limit of detectability of 2.5 μU/mL (Quest Diagnostics). HOMA-IR was calculated by dividing the product of insulin (μU/mL) and glucose (mg/dL) by 405 (18). The HOMA-IR cutoff point for diagnosis of insulin resistance was >= 3.16. (19). Following collection and processing, serum samples for AMH were stored at −20° C until hormone analyses were performed. Serum AMH was measured in duplicate using an ultrasensitive ELISA (Diagnostic Systems Laboratory, distributed by Beckman-Coulter) in accordance with the manufacturer's instructions. All serum AMH measurements were performed in the same lab using the same assay. The lower limit of detectability for this assay is 0.08 ng/mL. The intra-and interassay coefficients of variation were 7.29% and 2.75%, respectively.

Ultrasound Data

All PCOS subjects underwent transabdominal pelvic ultrasonography as part of their PCOS diagnostic workup. The images were obtained using a Phillips HDI 5000 ultrasound machine with a curved 5 mHz transducer. No ultrasound data was available for the control group. Ultrasound images were re-reviewed with a Pediatric Radiologist to confirm the reported measurements and to determine ovarian morphology. Ovarian volume was calculated as 0.5233 × length × width × thickness, derived from the formula for a prolate ellipsoid. An ovarian volume of 10 ml or more was considered enlarged. As transabdominal ultrasound limits follicle visualization, the number of follicles was described as "few" when fewer than 5, "moderate" when between 5 and 10, and "multiple" when greater than 10. Follicle distribution was described as central, peripheral, or mixed. The presence of cysts greater than 10 mm was noted.

Statistical Methods

A P value of <0.05 was considered significant. Comparisons of two groups on continuous variables were made using the Student t test; for comparisons of more than 2 groups, anova tests were used. The χ^2 tests were performed to assess the correlations between two categorical variables. The correlation between continuous variables was assessed using Pearson's correlation coefficient. All analyses were two-tailed and performed using SAS. Results are reported as mean ± SD.

Results

Clinical and demographic characteristics (Table 1)

There was no significant difference in mean age between the PCOS group (15.2 ±1.8 years) and controls (14.1± 1.7 years) (P = 0.08). BMI Z-score was similar in the PCOS group (2.07 ± 0.48) and controls (2.04 ± 0.25) (P = 0.84). The majority of subjects in both groups were Hispanic (78.26% of the PCOS group n = 18, 75% of the control group n = 9, P = 0.74). Of the remaining PCOS subjects, 3 were Asian and 2 were of mixed ethnicity. Of the remaining

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controls, one was Asian, one was African American, and one was Native American. The average age at menarche was similar between the PCOS group (11.6 ± 1.3 years) and controls (11.4 ± 1.5 years) ($P = 0.6$). Most PCOS subjects were oligo- or amenorrheic (91.3%) while the majority of control subjects had regular menses (91.67%) ($P < 0.0001$). One or more physical signs of hyperandrogenism (acne, alopecia, or male pattern baldness) was present in 86.96% of PCOS subjects compared with 41.67% of controls ($P = 0.0049$). There was no significant difference in the presence of acanthosis nigricans between the PCOS group (78.26%) and control group (87.82%) ($P = 0.8$).

Hormonal and biochemical profiles(Table 2)

Serum AMH was significantly higher in the PCOS group (6.78 +−3.55 ng/mL) compared with controls (3.38 +− 1.48 ng/mL) ($P = 0.0004$). No significant correlation existed between AMH and BMI Z-score (r = 0.11, $P = 0.6$) or fasting insulin (r = −0.00041, $P = 0.99$). There was a weak positive correlation between AMH and free Testosterone that did not reach statistical significance (r = 0.38, $P = 0.08$). The PCOS subjects had significantly higher free Testosterone levels (9.76 +−5.13 pg/mL) compared to controls (5 +−2.02 pg/mL) ($P = 0.0092$). Data on fasting insulin and glucose levels were available in 19 out of 23 PCOS subjects and 7 out of 12 control subjects. Of these, there was no significant difference in insulin resistance defined as a HOMA-IR >= 3.16 ($P = 0.53$). (19). The ratio of LH to FSH was greater than two in 9 out of 23 of the PCOS subjects versus 4 out of 12 controls ($P = 0.8$).

Ovarian ultrasound characteristics(Table 3)

Transabdominal pelvic ultrasound data was available for all PCOS subjects.

Ovarian Volume—Mean left ovarian volume was 9.75 ± 5.78 mL. Mean right ovarian volume was 9.55 ± 4.07 mL. Overall mean ovarian volume was 9.65 ± 4.58 mL. Ovarian volume was greater than 10 mL in 35% of images. Serum AMH positively correlated with ovarian volume (left ovary r = 0.65, $P = 0.0007$, right ovary r = 0.55, $P = 0.0065$).

Ovarian Morphology—Peripheral follicular distribution was noted in 76% of ultrasound images (n = 35). In the remainder, the follicular distribution was mixed (n = 11). Ultrasound imaging of the left ovary demonstrated a positive correlation between serum AMH and peripheral follicle distribution ($P = 0.0027$) No significant correlation existed between AMH and peripheral follicle distribution in ultrasound images of the right ovary ($P = 0.48$) In 38/46 ultrasound images, more than 10 follicles were noted. In the remainder, between 5 and 10 follicles were noted (83% of images demonstrated greater than 10 follicles). There was no significant correlation between AMH and follicle number ($P = 0.99$ on left ovarian images, $P = 0.8752$ on right ovarian images).

Discussion

The present study demonstrates that serum AMH positively correlates with ovarian volume in adolescent girls with PCOS. Ovarian volume is comprised of follicular and stromal volumes. Follicular volume reflects follicle number and size. Multiple studies have shown a positive relationship between serum AMH and follicle number in PCOS (13, 20,21) reflecting the known increased production of AMH by high numbers of preantral and antral follicles in polycystic ovaries (9). Our study did not demonstrate a positive correlation between serum AMH and follicle number likely because the majority of ultrasound images demonstrated multiple (greater than 10) follicles which could not be more precisely quantified due to the technical limitations inherent to transabdominal ultrasounds. It is

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probable that a larger sample size studied with higher definition transvaginal ultrasounds would have demonstrated a link between AMH and follicle number.

Even so, it has been shown that an increase in stromal volume is the foremost cause of ovarian enlargement in PCOS (22–25). Stromal volume mainly reflects theca cell mass. AMH exerts its effects by binding to a specific type II receptor, AMHR2 (26,27). Data demonstrates mRNA encoding AMHR2 in human theca cells (28,29). Although the causative effect of AMH on increased ovarian volume has not been established, it is possible that AMH, in addition to the known contributions of insulin (30), contributes to increased stromal volume in PCOS by binding to AMHR2 on theca cells and exerting downstream effects. Our finding of a positive correlation between serum AMH and ovarian volume may therefore support the existence of AMH mediated cross talk between ovarian granulosa and theca cells. (31) Peripheral follicular distribution is a frequent ovarian morphological characteristic of PCOS (32), seen in 76% of our study population and positively correlating with AMH levels in the left ovary. It is unclear why a positive correlation was not seen in the right ovary but it may be a result of our relatively small sample size. It is possible that AMH mediated stromal alterations contribute to this distinct morphological feature.

Polycystic ovary morphology is a cardinal feature of PCOS and thus an important diagnostic criterion. (3). Lack of ultrasound data may lead to underdiagnosis of PCOS (33). Ideally, transvaginal ultrasounds should be performed to optimize image resolution, particularly in obese patients such as those studied here and commonly found in PCOS. Transvaginal ultrasounds, however, are often unobtainable in adolescents due to their young age. A marker reflective of increased ovarian volume would therefore provide useful information to supplement or replace ovarian ultrasound in the diagnosis or follow up of PCOS, particularly in adolescents. The link between serum AMH and ovarian volume demonstrated in this study further supports the use of AMH as such a marker. The observed correlation between serum AMH and peripheral follicular distribution lends further credence to the use of elevated serum AMH as a reflection of ultrasound characteristics typical of PCOS.

Our data confirms other findings (15) that serum AMH is elevated in adolescents with PCOS compared with controls. It is unknown whether high serum AMH causes the disruption in ovulation characteristic of PCOS or is the result of disturbed folliculogenesis (34, 35). Studies suggest, however, that high serum AMH exerts a restrictive influence on follicular growth (36–38). AMH null mice have an increased transition from primordial to growing follicles and early exhaustion of the primordial follicle pool (39). Follicles exhibit increased sensitivity to FSH when AMH is absent, suggesting that AMH may have a negative effect on dominant follicle selection (40). Unfortunately, to date, most studies examining the intra-ovarian effects of AMH have been performed in rodents and may not be generalizable to humans. Regardless, our findings confirm that increased serum AMH appears to be an early and consistent characteristic of PCOS.

Data reporting the relationship between serum AMH and androgen levels have been conflicting. Multiple studies have demonstrated a positive correlation between androgen levels and serum AMH (12, 13, 41). A recent study on a large PCOS population using principal component analysis concluded that serum AMH may be used as a surrogate for markers of hyperandrogenism in diagnosing PCOS (42). Other studies, however, report no correlation between androgen levels and serum AMH (15, 43). As androgen levels fall with treatment or improvement in PCOS, serum AMH levels have not consistently been shown to decrease (44). Our results do not demonstrate a correlation between serum AMH and free testosterone levels. As AMH is known to inhibit aromatase (45), it has been proposed (31, 46) that intraovarian rather than serum androgen levels are more closely related to AMH. Similarly, there is no clear consensus on the relationship between insulin resistance and

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serum AMH. Our results are in line with other studies in finding no correlation between degree of insulin resistance and serum AMH (13, 41).

This pilot study did not benefit from the advantages inherent to a larger sample size. The retrospective nature of the study prevented the ascertainment of ultrasound data in controls and the timing of blood sampling with subjects' menstrual cycles. Multiple studies have shown no variation in serum AMH through the menstrual cycle (20, 47–49) indicating AMH production by preantral and antral follicles is gonadotropin independent and is not controlled by an ovarian-hypothalamic-pituitary feedback loop (46,50) These findings are substantiated by the lack of change in AMH levels despite gonadotropin suppression by pregnancy, oral contraceptive pills, and GnRH agonist therapy (51–55). Other studies of young women demonstrate a significant rise in AMH during the follicular phase of the cycle (56, 57) likely resulting from continued growth of small follicles (34). It therefore remains debateable whether AMH levels vary with the menstrual cycle and it is questionable whether the reported fluctuations are large enough to merit clinical significance (34). Until these questions are resolved, future studies of serum AMH should ideally be timed with subjects' menstrual cycles.

In conclusion, the positive relationship between serum AMH and ovarian volume unrelated to degree of obesity and insulin resistance support the use of serum AMH as a potential practical and effective independent marker to supplement ovarian ultrasound in the clinical diagnosis and follow up of PCOS. Our study and others demonstrate that elevated serum AMH appears to be a consistent feature of PCOS which is present in adolescents. Future larger, prospective studies are needed to confirm these results. Such studies should seek to elucidate the intra-ovarian effects of AMH and uncover the factors controlling AMH production and release by granulosa cells. Studies should examine the potential interplay between AMH and theca cell function, particularly whether AMH influences stromal volume and follicular morphology.

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References

1. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet. 2007; 370:685–697. [PubMed: 17720020]
2. Franks S. Polycystic ovary syndrome. N Engl J Med. 1995; 333:853–861. [PubMed: 7651477]
3. Ruutiiainen K, Erkkola R, Gronroos MA, Iriala K. Influence of body mass index and age on the grade of hair growth in hirsute women of reproductive age. Fertil Steril. 1988; 50(2):260–265. [PubMed: 3396696]
4. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop 2004 Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 81:19–25.
5. Josso N, Cate RL, Picard JY, Vigier B, di Clemente N, Wilson C, Imbeaud S, Pepinsky RB, Guerrier D, Boussin L, Legeai L, Carre-Eusebe D. Anti-mullerian hormone: the Jost factor. Recent Progress in Hormone Research. 1993; 48:1–59. [PubMed: 8441845]
6. Lee MM, Donahoe PK. Mullerian inhibiting substance: a gonadal hormone with multiple functions. Endocrine Reviews. 1993; 14:152–164. [PubMed: 8325249]
7. Pellatt L, Hanna L, Brincat M, Galea R, Brain H, Whitehead S, Mason HD. Granulosa cell production of anti-Mullerian hormone (AMH) is increased in the polycystic ovary syndrome. JCEM. 2007; 90:240–245. [PubMed: 17062765]

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8. Rajperts-de Meyts E, Jorgensen N, Graem N, Muller J, Cate RL, Skakkebaek NE. Expression of anti-Mullerian hormone during normal and pathological gonadal development: association with differentiation of Sertoli and granulosea cells. J Clin Endocrinol Metab. 1999; 84:3836–3844. [PubMed: 10523039]
9. Weenan C, Laven JS, Von Bergh AR, Caranfield M, Groome NP, Visser JA, Kramer P, Fauser BC, Themmen AP. Anti-Mullerian hormone expression pattern in the human ovary: potential implications for initial and cyclic follicle recruitment. Mol hum Reprod. 2004; 10:77–83. [PubMed: 14742691]
10. Lee MM, Donahoe PK, Hasegawa T, Silverman B, Crist GB, Best S. Mullerian-inhibiting substance in humans: normal levels from infancy to adulthood. J Clin Endocrinol Metab. 1996; 81:571–576. [PubMed: 8636269]
11. Hagen C, Aksglaede L, Sorensen K, Main K, Boas M, Cleemann L, Holm K, Gravholt C, Andersson AM, Pedersen A, Petersen JH, Linneberg A, Kjaergaard S, Juul A. Serum levels of anti-mullerian hormone as a marker of ovarian function in 926 healthy females from birth to adulthood and in 172 turner syndrome patients. J Clin Endocrinol Metab. 2010; 95(11):5003–5010. [PubMed: 20719830]
12. Laven J, Mulders A, Visser J, Themmen A, DeJong F, Fauser B. Anti-mullerian hormone serum concentrations in normoovulatory and anovulatory women of reproductive age. J Clin Endocrinol Metab. 2004; 89:318–323. [PubMed: 14715867]
13. Pigny P, Merlen E, Robert Y, Cortet-Rudelli C, Decanter C, Jonard S, DeWailly D. 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(12):5957–5962. [PubMed: 14671196]
14. Piltonen T, Morin-Papunen L, koivunen R, Perheentupa A, Ruoken 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. Human Reproduction. 2005; 20:1820–1826. [PubMed: 15802325]
15. Siow Y, Kives S, Hertweck P, Perlman S, Fallat M. Serum mullerian-inhibiting substance levels in adolescent girls with normal menstrual cycles or with polycystic ovary syndrome. Fertility and Sterility. 84(4):938–944. [PubMed: 16213847]
16. Park A, Lawson M, Chuan S, Oberfield S, Hoeger K, Witchel S, Chang R. Serum anti-mullerian hormone concentrations are elevated in oligomenorrheic girls without evidence of hyperandrogenism. J Clin Endocrinol Metab. 2010; 95(4):1786–1792. [PubMed: 20150576]
17. Crisosto N, Codner E, Maliqueo M, Echiburu B, Sanchez F, Cassorla F, Sir-Petermann T. Anti-mullerian hormone levels in peripubertal daughters of women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2007; 92(7):2793–2743. [PubMed: 17440010]
18. Quon MJ. Limitations of the fasting glucose to insulin ratio as an index of insulin sensitivity. J Clin Endocrinol Metab. 2001; 86:4615–4646. [PubMed: 11600512]
19. Keskin M, Kurtoglu S, Kendiirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics. 2005; 115(4):e500–e503. [PubMed: 15741351]
20. Fanchin R, Schonauer LM, Righini C, Guibourdenche J, Frydman R, Taieb J. Serum ant-Mullerian hormone is more strongly related to ovarian follicular status than serum inhibin B, estradiol, FSH and LH on day 3. Hum Reprod. 2003; 18:323–327. [PubMed: 12571168]
21. Van Rooij IA, Broekmans FJ, te Velde ER, Fauser BC, Bancsi LF, de Jong FH, Themmen AP. Serum anti-Mullerian hormone levels: a novel measure of ovarian reserve. Hum Reprod. 2002; 17:3065–3071. [PubMed: 12456604]
22. Balen A, Laven J, Tan SL, Dewailly D. Ultrasound assessment of the polycystic ovary: international consensus definitions. Human Reproduction Update. 2003; 9(6):505–514. [PubMed: 14714587]
23. Bucket WM, Bouzayen R, Watkin KL, Tulandi T, Tan SL. Ovarian stromal echogenicity in women with normal and polycystic ovaries. Human Reproduction. 1999; 14(3):618–621. [PubMed: 10221685]

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24. Dewailly D, Robert Y, Helln I, Ardaens Y, Thomas-Desrousseaux P, Lemaltre L, Fossati P. Ovarian stromal hypertrophy in hyperandrogenic women. Clinical Endocrinology. 1994; 41:557–562. [PubMed: 7828342]
25. Kyei-Mensah A, Tan SL, Zaidi J, Jacobs HS. Relationship of ovarian stromal volume to serum androgen concentrations in patients with polycystic ovary syndrome. Human Reproduction. 1998; 13:1437–1441. –increased stromal volume is the main cause of ovarian enlargement in PCOS. [PubMed: 9688367]
26. Imbeaud S, Faure E, Lamarre I, Mattei MG, di Clemente N, Tizard R, Carre-Eusebe D, Belville C, Tragethon L, Tragethon L, Tonkin C. Insensitivity to anti-Mullerian hormone due to a mutation in the human anti-Mullerian hormone receptor. Nature. 1995; 11:382–388.
27. Visser JA, McLusky A, van Beers T, Weghuis O, van Kessel AG, Grootegoed A, Themmen APN. Structure and chromosomal localization of the human anti-Mullerian hormone type II receptor gene. Biochemical and Biophysical Research Communications. 1995; 215:1029–1036. [PubMed: 7488027]
28. Ingraham HA, Hirokawa Y, Roberts LM, Mellon SH, McGee E, Nachtigal MW, Visser JA. Autocrine and paracrine Mullerian inhibiting substance hormone signaling in reproduction. Recent Progress in Hormone Research. 2000; 55:53–67. [PubMed: 11036933]
29. Hanna, L.; Pellatt, L.; Rice, S.; Whitehead, S.; Mason, HD. Anti-Mullerian hormone (AMH) production by and AMH type II receptor (AMHRII) in normal human ovaries; Presented at the 8th European Congress of Endocrinolgy; Glasgow, UK. 2006. Endocrine Abstracts 11 P687
30. Loverro G, Vicino M, Lorusso F, Vimercati A, Greco P, Selvaggi L. Polycystic ovary syndrome: relationship between insulin sensitivity, sex hormone levels and ovarian stromal blood flow. Gynecol Endocrinol. 2001; 15:142–149. [PubMed: 11379011]
31. Pellatt L, Rice S, Mason HD. Anti-mullerian hormone and polycystic ovary syndrome: a mountain too high? Reproduction. 2010; 139:825–833. [PubMed: 20207725]
32. Shah B, Parnell L, Milla S, Kessler M, David R. Endometrial thickness, uterine, and ovarian ultrasonographic features in adolescents with polycystic ovarian syndrome. Journal of pediatric & adolescent gynecology. 2010; 23(3):146–152. [PubMed: 19733099]
33. Broder-Fingert S, Shah B, Kessler M, Pawelczak M, David R. Evaluation of Adolescents for Polycystic Ovary Syndrome in an Urban Population. J Clin Res Ped Endo. 2009; 1(4):188–193.
34. La Marca A, Broekmans FJ, Volpe A, Fauser BC, Macklon NS. on behalf of the ESHRE Special Interest Group for Reproduction Endocrinology-AMH Round Table. Anti-mullerian hormone: what do we still need to know? Human Reproduction. 2009
35. Falbo A, Rocca M, Russo T, D'Ettore A, Tolino A, Zullo F, Orio F, Palomba S. Serum and follicular anti-Mullerian hormone levels in women with polycystic ovary syndrome (PCOS) under metformin. Journal of Ovarian Research. 2010; 3:16–21. [PubMed: 20663178]
36. Gigli I, Cushman RA, Wahl CM, Fortune JE. Evidence for a role for anti-Mullerian hormone in the suppression of follicle activation in mouse ovaries and bovine ovarian cortex grafted beneath the chick chorioallantoic membrane. Molecular Reproduction nad Development. 2005; 71:480–488.
37. Themmen AP. Anti-Mullerian hormone: its role in follicular growth initiation and survival and as an ovarian reserve marker. J Natl Cancer Inst Monogr. 2005; 34:18–21. [PubMed: 15784815]
38. Visser JA, Themmen AP. Anti-Mullerian hormone and folliculogenesis. Mol Cell Endocrinol. 2005; 234:81. [PubMed: 15836956]
39. Durlinger AL, Kramer P, Karels B, de Jong GH, Uilenbrock JT, Grootegoed JA, Themmen AP. Control of primordial follicle recruitment by anti-Mullerian hormone in the mouse ovary. Endocrinology. 1999; 140:5789–5796. [PubMed: 10579345]
40. Durlinger AL, Gruijters MJ, Kramer P, Karels B, Kumar TR, Matzuk MM, Rose UM, de Jong FH, Uilenbroek JT, Grootegoed JA, Themmen A. Anti-Mullerian hormone attenuates the effects of FSH on follicle development in the mouse ovary. Endocrinology. 2001; 142:4891–4899. [PubMed: 11606457]
41. Eldar-Geva T, Margalioth EJ, Gai M, Ben-Chetrit A, Algur N, Zylber-Haran E, Brooks B, Huerta M, Spitz IM. Serum anti-Mullerian hormone levels during controlled ovarian hyperstimulation in women in polycystic ovaries with and without hyperandrogenism. Human Reproduction. 2005; 20:1814–1819. [PubMed: 15802320]

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42. Dewailly D, Pigny P, Soudan B, Catteau-Jonard S, Decanter C, Poncelet E, Duhamel A. Reconciling the Definitions of Polycystic Ovary Syndrome: The Ovarian Follicle Number and Serum Anti-Mullerian Hormone Concentrations Aggregate with the Markers of Hyperandrogenism. J Clin Endocrinol Metab. 2010; 95(9):4399–4405. [PubMed: 20610596]
43. La Marca A, Orvieto R, Giulini S, Jasonni VM, Volpe A, De Leo V. Mullerian-inhibiting substance in women with polycystic ovary syndrome: relationship with hormonal and metabolic characteristics. Fertility and Sterility. 2004; 82:970–972. [PubMed: 15482785]
44. Carlson SM, Vanky E, Fleming R. Anti-Mullerian hormone concentrations in androgen-suppressed women with polycystic ovary syndrome. Hum Reprod. 2009; 24:1732–1738. [PubMed: 19342396]
45. Pellatt, L.; Rice, S.; Brincat, M.; Galea, R.; Mason, H. Anti-Mullerian hormone (AMH) inhibits aromatase expression in granulose cells from human ovaries; Proceedings of the Endocrine Society USA, 89th Annual Meeting; Toronto. 2007. Canada Oral Presentation 48-4
46. Visser JA, de Jong F, Laven J, Themmen A. Anti-Mullerian hormone: a new marker for ovarian function. Reproduction. 2006; 131:1–9. [PubMed: 16388003]
47. Cook CL, Siow Y, Taylor S, Fallat ME. Serum Mullerian-inhibiting substance levels during normal menstrual cycles. Fertil Steril. 2000; 73:859–861. [PubMed: 10731554]
48. Hehenkamp WJ, Looman CW, Themmen AP, de Jong FH, Te Velde ER, Broekmans FJ. Anti-Mullerian hormone levels in the spontaneous menstrual cycle do not show substantial fluctuations. J Clin Endocrinol Metab. 2006; 91:4057–4063. [PubMed: 16804046]
49. La Marca A, Malmusi S, Giulini S, Tamaro LF, Orvieto R, Levratti P, Volpe A. Anti-Mullerian hormone plasma levels in spontaneous menstrual cycle and during treatment with FSH to induce ovulation. Hum Reprod. 2004; 19:2738–2741. [PubMed: 15459174]
50. Ledger W. Clinical utility of measurement of anti-mullerian hormone in reproductive endocrinology. J Clin Endocrinol Metab. 2010; 95(12):5144–5154. [PubMed: 21131535]
51. La Marca A, Giulini S, Orvieto R, De Leo V, Volpe A. Anti-Mullerian hormone concentrations in maternal serum during pregnancy. Hum Reprod. 2005; 20:1569–1572. [PubMed: 15734752]
52. Mohamed KA, Davies WA, Lashen H. Antimullerian hormone and pituitary gland activity after prolonged down-regulation with goserelin acetate. Fertil Steril. 2006; 86:1515–1517. [PubMed: 16978621]
53. Arbo E, Vetori DV, Jimenez MF, Freitas FM, Lemos N, Cunha-Filho JS. Serum anti-Mullerian hormone levels and follicular cohort characteristics after pituitary suppression in the late luteal phase with oral contraceptive pills. Hum Reprod. 2007; 22:3192–3196. [PubMed: 17981819]
54. Somunkiran A, Yavuz T, Yucel O, Ozdemir I. Anti-mullerian hormone levels during hormonal contraception in women with polycystic ovary syndrome. Eur J Obstet Gynecol Reprodu Biol. 2007; 134:196–201.
55. Streuli I, Fraisse T, Pillet C, Ibecheole V, Bischof P, de Ziegler D. Serum antimullerian hormone levels remain stable throughout the menstrual cycle and after oral or vaginal administration of synthetic sex steroids. Fertil Steril. 2008; 90:395–400. [PubMed: 17919608]
56. Sowers M, McConnell D, Gast K, Zheng H, Nan B, McCarthy JD, Randolph JF. Anti-Mullerian hormone and inhibin B variability during normal menstrual cycles. Fertil Steril. 2009
57. Wunder DM, Bersinger NA, Yared M, Kretschmer R, Birkhauser MH. Statistically significant changes of antimullerian hormone and inhibin levels during the physiologic menstrual cycle in reproductive age women. Fertil Steril. 2008; 89:927–933. [PubMed: 17603052]

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Table 1

Demographic and clinical characteristics of PCOS subjects and obese controls

	PCOS	Controls	*P*
n	23	12	
Age (years)	15.2 ± 1.84	14.08 ± 1.7	0.08
Ethnicity			0.74
Hispanic	18	9	
Asian	3	1	
Other *	2	2	
BMI (kg/m^2) *Z* Score	2.07 ± 0.48	2.04 ± 0.25	0.84
Age at menarche (years)	11.63 ± 1.31	11.35 ± 1.45	0.6
Menstrual history			0.0001
Regular	2	11	
Oligomenorrheic	14	1	
Amenorrheic	7	0	
Acne present	15	8	0.18
Hirsute	17	0	0.0001
Acanthosis nigricans present	18	10	0.8

Data are expressed as mean ± SD.

* Other = African American, Native American, or mixed ethnicity

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Table 2

Hormonal and biochemical profiles of PCOS subjects and controls

	n	PCOS	n	Controls	*P* value
AMH (ng/mL)	23	6.78 ± 3.56	12	3.38 ± 1.48	0.0004
Free Testosterone (pg/mL)	23	9.76 ± 5.14	6	5 ± 2.84	0.0092
fasting glucose (mg/dL)	19	88.63 ± 12.82	10	89.2 ± 8.61	0.89
fasting insulin (μU/L)	19	21.12 ± 10.5	7	18.96 ± 7.61	0.58
HOMA-IR	19	4.79 ± 2.45	7	4.55 ± 1.43	0.53

Data expressed as mean ± SD.

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Table 3

Pelvic ultrasound characteristics of PCOS group

Ovarian Volume (mL)	
Right ovarian volume	9.55 ± 5.78
Left ovarian volume	9.75 ± 4.07
Mean ovarian volume	9.65 ± 4.58
Follicle Distribution (%)	
Peripheral	76%
Mixed	24%
Follicle Number	
Few	0
Moderate	17
Multiple	83

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Table 4

Correlation between serum AMH and PCOS subjects' pelvic ultrasound indices, degree of obesity, and hormonal data

	r	*P*
Ultrasound indices		
Left ovarian volume	0.65	0.0007
Right ovarian volume	0.55	0.0065
Mean ovarian volume	0.66	0.0007
Degree of obesity		
BMI *Z* Score	0.11	0.6
Hormonal data		
Free testosterone (pg/mL)	0.38	0.08
Fasting insulin (μU/mL)	0.00041	0.99