

DO THE ANTI-MULLERIAN HORMONE LEVELS OF ADOLESCENTS WITH POLYCYSTIC OVARIAN SYNDROME, THOSE WHO ARE AT RISK FOR DEVELOPING PCOS, AND THOSE WHO EXHIBIT ISOLATED OLIGOMENORRHEA DIFFER FROM THOSE OF ADOLESCENTS WITH NORMAL MENSTRUAL CYCLES?

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INTRODUCTION

An elevated anti-Müllerian hormone (AMH) level might serve as a noninvasive screening or diagnostic test for polycystic ovarian syndrome (PCOS) in adolescents, although no well-defined cut-offs have been described. We explored whether the AMH levels of adolescents with PCOS, those at risk of developing PCOS, and those who exhibited isolated oligomenorrhea (OM), differed from those of adolescents with normal menstrual cycles, and we identified an AMH level that was potentially diagnostic of PCOS.

METHODS AND RESULTS

A diagnosis of PCOS was based on the 2012 Amsterdam (ESHRE/ASRM) criteria:

- 1) Clinical and biochemical hyperandrogenism,
- 2) OM or amenorrhea persisting for 2 years after menarche,
- 3) The presence of one ovary $\leq 10 \text{ cm}^3$ in volume and/or the presence of ≥ 12 follicles 2–9 mm in diameter in each ovary. Hyperandrogenism was diagnosed if hirsutism was evident (Ferriman–Gallwey score ≥ 8) and/or the serum testosterone level was elevated. Such an elevation was defined as a total testosterone level $>51 \text{ ng/dL}$. OM was defined as an average menstrual cycle length of 45–90 d; the normal menstrual interval is 21–45 d in young females.

Table 2. Laboratory findings of all groups

	PCOS (n=21)	PCOS risk (n=20)	OM (n=21)	NMC (n=30)
FSH (mIU/ml)	5.24±1.87	4.76±0.93	5.8±1.81	5.9±2.41
E ₂ (pg/ml)	76.5±39.2	40.2±18.5	61.2±34.9	57±61.8
f-testosterone (pg/ml)	3.02±1.93	2.36±0.94	2.62±0.85	3.01±4.25
SHBG (nmol/L)	57.8±63.5	47.8±46.6	34.4±18	42.5±29.3
LH (mIU/ml)	14.4±12.2 ^{a,c}	7.72±4.65	12.0±7.8 ^{f,g}	7.33±8.53
t-testosterone (ng/dl)	78.3±28.8 ^{a,b,c}	62.8±18.4 ^{d,e}	49.4±17.2	37.7±20.9
1,4-androstenedione (ng/ml)	4.49±2.38 ^{a,c}	3.08±1.72	3.51±1.41	2.79±1.6
AMH (ng/ml)	9.29±5.17 ^{b,c}	7.59±4.87 ^e	6.45±3.23 ^f	4.26±3.43

The AMH levels of the PCOS and the “at-risk-of-PCOS” risk groups were similar and AMH levels of the PCOS group were significantly higher than those of the OM and NMC groups ($p=0.001$). The AMH level of the “at-risk-of-PCOS” group was similar to that of the OM group but significantly higher than that of the NMC group. This level was significantly higher in the OM than in the NMC group ($p=0.001$) (Table 2).

^a $p<0.05$ for PCOS vs. PCOS risk
^b $p<0.05$ for PCOS vs. OM
^c $p<0.05$ for PCOS vs. NMC
^d $p<0.05$ for PCOS risk vs. OM
^e $p<0.05$ for PCOS risk vs. NMC
^f $p<0.05$ for OM vs. NMC
^g $p<0.05$ for OM vs. PCOS risk

The PCOS group consisted of individuals meeting all three diagnostic criteria; those in the “at-risk-of-PCOS” group met two of the criteria. The OM group consisted of those with isolated OM who did not satisfy the other PCOS diagnostic criteria.

Table 1. Baseline demographic, clinical characteristics of all groups

	PCOS (n=21)	PCOS risk (n=20)	OM (n=21)	NMC (n=30)	P
Chronological age (year)	15.7±1.58	15.8±1.61	15.8±0.88	16.0±1.84	0.961
Menarche age	11.9±0.89	11.8±1.06	11.9±2.34	12.3±1.17	0.648
Birth weight (gr)	3288±553	2878±1062	3237±330	3048±559	0.349
Gestational age (week)	38±1.03	37.3±2.78	39.5±3.2	36.9±1.03	0.261
Height (cm)	160.6±7.6	160±7.42	160±5.09	157.2±6.2	0.243
Height SDS	-0.23±1.62	-0.19±0.96	-0.46±0.86	-0.77±1.1	0.313
Weight (kg)	59.6±25.4	73.7±20.7	68.5±16.9	63.9±16	0.152
BMI (kg/m ²)	24.06±7.0	28.5±6.54	26.5±6.05	24.1±8.84	0.177
BMI SDS	0.56±1.79 ^a	2.23±1.63 ^a	1.56±1.49	1.14±1.58	0.047

^a $p<0.05$ for PCOS vs. PCOS risk

Table 3. Ovarian size and number of follicles in four groups

	PCOS (n=21)	PCOS risk (n=20)	OM (n=21)	NMC (n=30)	P
Right ovarian volume (ml)	14.9±6.98	12.0±6.2	7.96±4.03	9.83±5.74	0.002
Left ovarian volume (ml)	14.9±8.2	11.4±4.27	8.09±2.98	8.72±4.08	0.000
Follicle number	9.57±3.51	8±4.56	7.42±4.57	7.71±4.32	0.409

The sensitivity and specificity of each serum AMH concentration for identifying PCOS and “at-risk-of-PCOS” subjects were determined by ROC curve analysis. The specificity at a cut-off value of 7.25 ng/mL was 83.3%, and the sensitivity was 58.5% (area under the curve [AUC] = 0.700; 95% CI 0.591–0.808; $p=0.001$). The positive and negative predictive values of this cut-off were 82.8% and 59.5%, respectively.

In the PCOS group only, significant positive correlations were evident between LH level and t-testosterone ($r=0.697$), f-testosterone ($r=0.838$), and 1,4-androstenedione ($r=0.770$) levels ($p<0.001$). Similarly, a significant negative correlation was evident between AMH level and the BMI SD in only the PCOS group ($r=-0.648$, $p<0.001$). No significant correlation was apparent between AMH level and ovarian volume or between AMH level and follicle number in any group.

DISCUSSION

An AMH cut-off of 7.25 ng/mL can assist in PCOS diagnosis in adolescents. However, before this criterion is used routinely, larger populations should be studied. OM subjects should be monitored for the development of PCOS.

