

Association between Weight Loss in Obese Indian Adolescent Girls with Polycystic Ovarian Syndrome and Decline in Anti-Müllerian Hormone Concentrations

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ABSTRACT

Objective: Several studies have reported anti-Müllerian hormone (AMH) concentrations in girls with polycystic ovarian syndrome (PCOS), but longitudinal studies of changes in AMH concentrations in relation to change in weight status are lacking in Indian adolescent girls with PCOS. Our objective was to study the longitudinal changes in AMH concentrations in obese Indian adolescent girls with PCOS with respect to weight loss.

Materials and methods: This longitudinal study was conducted at the adolescent clinic of Shrikhande Hospital and Research Centre Pvt Limited, Nagpur, India, from January 2017 to December 2017. 120 obese girls aged 13–19 years (50% with PCOS) were included in the study after obtaining informed consent. Girls with and without PCOS were matched to age, BMI, and weight status. Serum AMH, gonadotropins, testosterone, and oestradiol levels were determined. The intervention consisted of promoting physical activity, delivering nutrition education, and behavior therapy. Normal distribution was tested by the Kolmogorov–Smirnov test for all variables. The primary outcome was the change in AMH concentrations over time.

Results: Obese girls with PCOS demonstrated significantly ($p < 0.001$) higher AMH concentrations (5.7 ± 3.1 ng/mL) as compared to obese girls without PCOS (2.4 ± 1.3 ng/mL). Participants who had experienced weight loss were found to have significantly lower baseline AMH levels (-1.3 ± 1.8 ng/mL, $p = 0.04$). An association was also found between degree of weight loss and a decline in AMH levels, with subjects experiencing more weight loss demonstrating a higher decline in AMH level (-10.5 ± 1.1 kg vs -4.0 ± 1.0 kg; $p = 0.001$).

Conclusion: Anti-Müllerian hormone was increased in Indian obese adolescent girls with PCOS and decreased with weight loss.

Keywords: Anti-Müllerian hormone, Adolescent girls, Polycystic ovarian syndrome, Weight loss.

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INTRODUCTION

Polycystic ovarian syndrome is a heterogeneous syndrome classically characterized by features of anovulation (amenorrhoea, oligomenorrhoea, and irregular cycles) combined with symptoms of androgen excess (hirsutism, acne, and alopecia) as well as polycystic ovaries.^{1,2} It typically presents during adolescence. Anti-Müllerian hormone has been reported as a surrogate marker of antral follicles, which are the origins of hyperandrogenism in PCOS.³ Therefore, AMH may be useful for the diagnosis of PCOS.

The changes in AMH over time related to changes in weight status and hyperandrogenism have been analyzed in adult women. However, the findings are controversial. Some studies have reported that AMH concentrations are elevated in women with PCOS and decreased with dieting^{4,5} and exercise⁶ while other studies have demonstrated no effect.⁷ Several studies have reported AMH concentrations in girls with PCOS.^{8–10}

The longitudinal studies of changes in AMH concentrations in relation to change in weight status are lacking in Indian adolescent girls with PCOS. The objective in this study was to analyze the changes in AMH concentrations in obese Indian adolescent girls with PCOS with respect to weight loss.

MATERIALS AND METHODS

The period of the study was January 2017–December 2017. This longitudinal study was conducted at the adolescent clinic of Shrikhande Hospital and Research Centre Pvt Limited, Nagpur, India. 120 obese girls aged 13–19 years (50% with PCOS) were included in the study after obtaining informed consent. Inclusion criteria

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were evidence of anovulation, hyperandrogenism, either clinical or biochemical, and USG evidence of polycystic ovaries. Exclusion criteria were those who were not willing for blood collection and those on oral contraceptive pills.

The body mass index (BMI) of all participants was computed (weight in kg/square of height in meters). Obesity was defined as BMI of 30 or more. The diagnosis of the PCOS was applied according to the Rotterdam ESHRE/ASRM-Sponsored PCOS Workshop Group revised 2003 consensus criteria.

Girls with and without PCOS were matched to age, BMI, and weight status. Serum AMH, gonadotropins, testosterone, and oestradiol levels were determined. Serum AMH concentration was determined by a one-step enzyme immunoassay sandwich method with a final fluorescent detection (VIDAS® AMH assay). Serum testosterone, estradiol, and gonadotropin concentrations

were determined using a competitive immunoassay employing chemiluminescent technology (ADVIA Centaur CP system).

The intervention consisted of promoting physical activity, delivering nutrition education, and behaviour therapy for the girl and her family. The education was provided by a multidisciplinary team of pediatricians, dieticians, and psychologists.

Normal distribution was tested by the Kolmogorov–Smirnov test for all variables. The primary outcome was the change in AMH concentrations with respect to time.

Baseline variables and changes were correlated to AMH using Spearman correlation. Multiple regression analyses adjusted for baseline BMI and age were computed with AMH as the dependent variable and androgens, gonadotropins, and estradiol as independent variables.

RESULTS

Obese girls with PCOS demonstrated significantly ($p < 0.001$) higher AMH concentrations (5.7 ± 3.1 ng/mL) as compared to obese girls without PCOS (2.4 ± 1.3 ng/mL) (Figs 1 and 2).

Participants who had experienced weight loss were found to have significantly lower baseline AMH levels (-1.3 ± 1.8 ng/mL, $p = 0.04$). An association was also found between degree of weight

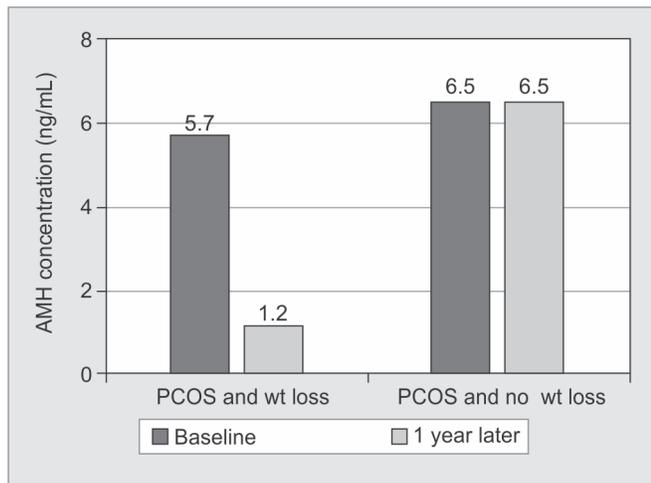


Fig. 1: AMH concentrations in obese girls with PCOS with and without weight loss

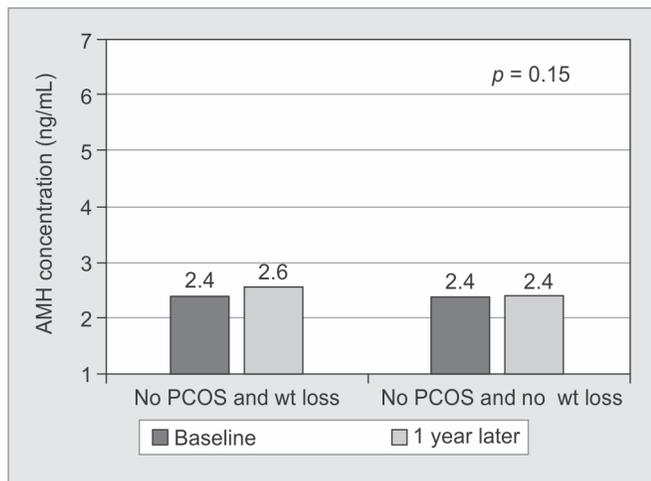


Fig. 2: AMH concentrations in obese girls without PCOS with and without weight loss

Table 1: Baseline correlations (r) between AMH, gonadotropins, and androgens (Spearman correlations) in 120 obese girls with and without PCOS

	Entire cohort ($n = 120$)	PCOS ($n = 60$)
LH	0.47	0.33
FSH	-0.05	-0.2
LH/FSH ratio	0.49***	0.35*
Testosterone	0.46**	0.42*
Estradiol	-0.42**	-0.39*

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

loss and decline in AMH levels, with subjects experiencing more weight loss demonstrating higher decline in AMH level (-10.5 ± 1.1 kg vs -4.0 ± 1.0 kg; $p = 0.001$).

Anti-Müllerian hormone level was significantly related to testosterone (cross-sectional: b -coefficient 3.5 ± 1.8 , $p = 0.001$; longitudinal: b -coefficient 0.52 ± 0.37 , $p = 0.02$) and luteinizing hormone (LH) (cross-sectional: b -coefficient 0.05 ± 0.04 , $p = 0.04$; longitudinal: b -coefficient 0.005 ± 0.004 , $p = 0.04$) but not to any other analysed parameter in multiple linear regression analyses (Table 1).

DISCUSSION

We were able to validate that the AMH concentrations were higher in obese Indian adolescent girls with PCOS as compared to obese girls without PCOS of similar age and BMI. It was also demonstrated that AMH concentrations returned to normal values in PCOS girls with weight loss. These findings align with most studies in adults with PCOS. Nybacka et al. showed decreased AMH concentrations during dieting in 57 overweight/obese women with PCOS.⁵ In a pilot study by Moran et al., it was demonstrated that exercise over a 12-week duration was associated with a decrease in AMH in 15 women with PCOS.⁶ There have been other studies which could not establish any change in AMH concentrations during lifestyle intervention in obese adult women with PCOS⁷ and a study by Vosnakis et al. actually documented increased AMH in 61 women with PCOS who were treated with orlistat, diet, and physical exercise.¹¹ The most likely explanation for these disparities could be the different study periods. It is possible that short interventions are insufficient for decline in AMH concentrations to occur, as proposed by Gougeon et al. that at least 3 months are required for the recruitment of a new antral follicle cohort once androgen and insulin values return to normal.¹²

In line with the multiple previous studies, AMH and LH concentrations were found to correlate positively in cross-sectional and longitudinal analyses in this study.^{13,14} Therefore, it is plausible that LH may be the initiator of rising AMH levels in PCOS, possibly via enhancing the synthesis of androgens.¹⁴ We also noted positive correlation between the serum AMH concentrations and the serum androgen concentrations in cross-sectional and longitudinal analyses, in concordance with the studies in adult patients.⁷ Together, these observations suggest early antral follicles in the ovary as the culprits of hyperandrogenism in PCOS.

Follicle stimulating hormone (FSH) and AMH are markers of functional ovarian reserve; however, they represent different stages of folliculogenesis.¹⁵ AMH concentration is a sensitive marker of the early antral follicle number,⁴ while FSH mostly reflects follicular maturation in the last 2 weeks, when follicles are gonadotropin sensitive.¹⁶ We could not find a significant relationship between FSH and AMH and this is consistent with

the study by Sir-Petermann et al.,¹⁷ while an inverse relation between AMH and serum FSH concentrations was demonstrated by Olszanecka-Glinianowicz et al.¹⁸ Anti-Müllerian hormone regulates follicle growth through the inhibition of FSH-dependent aromatase in granulosa cells.¹⁹ As oestrogens are transformed from androgens by this aromatase, there have been studies in women with PCOS that reported negative association between AMH and oestradiol concentrations.²⁰ In our study of Indian adolescent girls with PCOS, we found a significant negative relationship between oestradiol and AMH concentrations.

It was also noted that baseline AMH concentrations were higher in PCOS girls with weight loss compared to PCOS girls without weight loss during lifestyle intervention, while the girls did not differ according to androgens or gonadotropins at baseline.

This finding leads to the idea that the PCOS girls without weight loss manifest a more severe phenotype of the disease.

Our study presents some potential limitations. First, BMI is only an indirect measurement of fat mass. Additionally, a single measurement of LH and FSH as in our study provides little diagnostic sensitivity as gonadotropin concentrations are released in a pulsatile fashion into the circulation and vary during the menstrual cycle. Finally, the diagnosis of PCOS is a challenge in adolescents. However, the age and symptoms of our patients were similar to adolescent girls suffering from PCOS.

CONCLUSION

Anti-Müllerian hormone was increased in Indian obese adolescent girls with PCOS and decreased with weight loss. Anti-Müllerian hormone is longitudinally related to hyperandrogenism.

CLINICAL SIGNIFICANCE

Anti-Müllerian hormone measurement may be utilized as a more objective marker of PCOS in obese Indian adolescent girls as compared to ultrasonography which is a more subjective assessment and fraught with difficulties. Decline in AMH level with weight loss correlates with clinical and biochemical evidence of improvement of the disease phenotype.

MANUFACTURER NAME

- VIDAS® AMH assay (BioMérieux, Marcy-l'Étoile, France)
- ADVIA Centaur CP system (Siemens Healthineers, Erlangen, Germany)

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