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Does body mass index affect anti-mullerian hormone levels in girls and adolescents?

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Short title: Does BMI affect AMH levels in girls and adolescents?

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ABSTRACT

Anti-mullerian hormone (AMH) is a dimeric glycoprotein which belongs to the transforming growth factor-beta superfamily. In women, it is produced by granulosa cells in pre-antral and small antral follicles. In recent years, there has been a continuous increase in obesity among children and adolescents. There are few studies that present AMH concentrations in premenarcheal and early postmenarcheal girls. The purpose of this work is to assess whether AMH levels were associated with body mass index (BMI) in adolescent girls before and after menarche. The study was performed at the Pediatric Endocrinology Department and Outpatient Clinic at Upper Silesian Child Health Center. 82 girls were enrolled to the study. Body mass index seems not to affect the AMH levels in adolescents, however a special attention must be given when interpreting AMH levels in girls with irregular menstrual cycles and observed for PCOS.

Key words: AMH; BMI; obesity; adolescents; pediatric endocrinology

INTRODUCTION

Anti-mullerian hormone (AMH) is a dimeric glycoprotein which belongs to the transforming growth factor-beta superfamily. In male fetuses, it is produced by the Sertoli cells and induces regression of Mullerian ducts. In women, it is produced by granulosa cells in pre-antral and small antral follicles.

In recent years, there has been a continuous increase in obesity among children and adolescents. According to WHO data, if the current trend continues, 177 million people will be overweight and 91 million will be obese in the group of 5–17-year-olds by the year 2025. There is a connection between obesity and various endocrinologic disorders in girls, such as premature puberty, irregular menstrual cycles, developing polycystic ovary syndrome, infertility in future [1–3]. What is more, data show that androgen levels are higher in obese that lean girls during puberty [4].

The purpose of this work is to assess whether AMH levels were associated with body mass index (BMI) in adolescent girls before and after menarche.

MATERIAL AND METHODS

The study was performed at the Pediatric Endocrinology Department and Outpatient Clinic at Upper Silesian Child Health Center between 1 June 2019 and 31 March 2020. The subjects were consecutive girls who were referred to the Clinic (n = 100) for diagnostic process. The exclusion criteria were: (1) thyroid, prolactin, androgen, cortisol level disorders; (2) chronic systemic illness; (3) eating disorders; (4) smoking or drug or alcohol use; (5) taking medications known to interfere with reproductive hormones/receiving hormonal treatment. Eighteen girls were excluded from the study and 82 girls were enrolled to undergo further research.

Procedures

All the girls underwent physical examination, gynecological ultrasound, medical history and biochemical tests. Age at menarche was obtained retrospectively. Height was assessed to the nearest 0.1 cm and weight to the nearest 0.1 kg. Body mass index (BMI) was calculated for each girl using the standard formula [weight (kg) divided by height (m) squared]. The BMI Z-score and BMI percentile for each girl were calculated (https://zscore.research.chop.edu/calcbmi.php). Girls with BMI < 90 percentile were considered to have normal weight, girls with BMI ≥ 90 were considered to be overweight/obese (obesity was assessed ≥ 97 percentile).

The gynecological ultrasounds were performed transabdominally, always by the same experienced physician (Prof, PhD). The length, width and volume of the ovaries were measured. Uterus and cervix measurements were also taken. Transabdominal ultrasound was performed with a transabdominal probe using a Samsung ultrasound scanner.

Information about regularity of menstruation in menstruating girls was obtained. Cycle length was assessed according to the mean length of the last three menstrual cycles. Irregular menstrual cycles were considered as: (1) cycles 21–45 days in the period of 1–3 years after menarche, (2) cycles < 21 or > 35 days after 3 years from menarche, or < 8 menstruations in a year time, (3) cycles > 90 days in the period < 1 year from menarche [5].

Biochemical assays

Fasting blood samples were drawn from an antecubital vein between 8 am and 10 am for determination of luteinizing hormone (LH), follicle-stimulating hormone (FSH), total testosterone (TTE), inhibin B and AMH. The samples were centrifuged and stored at –20°C until analyses were conducted. TTE, LH, FSH, and AMH were measured with the electrochemiluminescence "ECLIA" method (Elecys, Roche Diagnostics GmbH, Mannheim). Inhibin B was measured with an enzyme-linked immunosorbent assay (ELISA Genie ELISA). In postmenarcheal girls, the samples were drawn between the 2^{nd} and 5^{th} day of their menstrual cycle (follicular phase). All biochemical assays were performed in the Laboratory of the Upper Silesian Child Health Center, Katowice, Poland.

Statistical analysis

Statistical analysis was performed using StatSoft Statistica version 13.3 software. Quantitative variables are presented as a mean and standard deviation (SD) or median and interquartile range (IQR). The qualitative variables are presented as an absolute value and/or percentage. The between-group differences for quantitative variables were verified using a parametric (t-test or ANOVA) or non-parametric tests (U Mann-Whitney or Kruskal-Wallis), with previous verification of their distribution by the Shapiro-Wilk or Smirnov-Kolmogorov tests. In the case of qualitative variables, the chi-square test or Fisher's exact test was used. A p value of < 0.05 was considered significant.

The study was approved by the Ethics Committee of Medical University of Silesia (KNW/0022/KB1/3/19).

RESULTS

The median age was 142 months (11 years and 10 months) (IQR 111–180). Of the 82 subsects included to the study, 59 had normal BMI and 23 were overweight or obese. Thirty girls were after menarche, while 52 girls had not menstruated yet. Among menstruating girls, 11 had irregular menstrual cycles. Table 1 presents biochemical results in girls enrolled to the study.

Table 1. Laboratory data and comparison of the groups (girls with normal BMI/ girls with excess weight)

	Total (n = 82)	Normal BMI (n = 59)	Overweight/ obese (n = 23)	p value
AMH [pmol/L]	30.47 ± 21	30.25 ± 20.38	31.03 ± 28.62	0.69
LH [mIU/mL]	4.76 ± 6.6	4.11 ± 5.86	6.43 ± 8.11	0.24
FSH [mIU/mL]	3.91 ± 4	3.58 ± 2.48	4.75 ± 6.47	0.92
TTE [ng/dL]	18.62 ± 21	18.13 ± 21.25	19.87 ± 20.73	0.36
Inhibin B [ng/mL]	0.45 ± 2	0.57 ± 2.34	0.14 ± 0.69	0.4

BMI — body mass index; AMH — anti-mullerian hormone; LH — luteinizing hormone; FSH — follicle-stimulating hormone; TTE — total testosterone

There were no statistically important differences between AMH levels in menstruating and non-menstruating girls depending on BMI (Tab. 2).

Table 2. Anti-mullerian hormone (AMH) levels [pmol/L] in menstruating and non-menstruating girls depending on body mass index (BMI)

	TOTAL	Normal BMI	Overweight/ obese	p value
Menstruating girls	39.59 ± 19.67	37.8 ± 24.16	43.17 ± 36.95	0.84
Non-menstruating girls	25.2 ± 16.93	26.37 ± 17.23	21.68 ± 16.15	0.3

DISCUSSION

Data concerning the connection between BMI and AMH levels in women remain inconsistent [6]. In our study, we did not find a relationship between AMH levels and presence of obesity/overweight. This may indicate that in girls, the BMI does not affect the AMH levels, so AMH may be used in endocrinologic diagnostics in both, girls with normal weight and girls with excess weight. Due to small group of menstruating girls, we were

unable to study the connection between AMH levels and irregularity of menstrual cycles. Kriseman et al. report that there was no correlation between BMI and AMH levels in their general clinic population, however they found out that AMH levels were inversely related to BMI in population with PCOS [7]. Cengiz et al. studied the relationship between AMH and BMI in girls with PCOS. They did not find the difference in serum AMH between obese and non-obese adolescent patients with PCOS [8].

The literature focuses on the association between BMI levels and AMH in women with polycystic ovarian syndrome [7–9]. As irregular menstrual cycles occur often in adolescents, the diagnosis of PCOS among them is challenging and should be made carefully, at least two years after menarche and modifications of the Rotterdam criteria should be implemented (biochemical hyperandrogenism, oligomenorrhoea at least two years after menarche, ovarian volume > 12mL and three conditions must be met) [5]. That is why in this work we were unable to examine whether there is a connection between AMH and BMI in girls with PCOS.

CONCLUSIONS

BMI seems not to affect the AMH levels in adolescents, however a special attention must be given when interpreting AMH levels in girls with irregular menstrual cycles and observed for PCOS.

Conflict of interest

The authors declare no conflict of interest.

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