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Anti-Mullerian hormone level in relation to physical activity and reproductive determinants in North Iranian infertile women

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Abstract

Introduction: Female infertility is responsible for approximately half of all cases of infertility and one of the causes of infertility in women is related to ovarian disorders. Anti-Müllerian Hormone (AMH) is one of the clinical markers of ovarian reserve. Physical activity may affect the reproductive system and AMH concentration in serum. We aim to evaluate the relationship between physical activity and reproductive determining fertility and anti-mullerin hormone (AMH) in infertile women in northern Iran.

Materials and Methods: This cross-sectional study included 234 women aged 18–45 referred to the Infertility Clinic of the Al-Zahra Hospital, Rasht, Iran. The reproductive characteristics and the amount of physical activity of the patients were recorded. Exclusion criteria included menopause, cancer, underlying endocrine diseases, use of hormonal drugs, diagnosis of PCOS based on Rotterdam criteria, any ovarian and uterine surgery, and endometriosis.

Results: As expected, we observed significantly lower AMH concentrations in older participants. There was no association between reproductive determinants and AMH level (P> 0.05). We observed lack of physical activity as well as vigorous physical activity, is associated with lower AMH concentration (P= 0.025, and P= 0.039 respectively).

Conclusion: In this study, AMH levels appear to be significantly lower in patients with a lack of physical activity as well as vigorous physical activity. The results of this study showed that by improving lifestyle, including the appropriate amount of physical activity, it may be possible to improve the results of infertility treatments. However, a larger study is needed to verify the findings of this study.

Keywords: Anti-Mullerian hormone, AMH, Female infertility, Physical activity, Lifestyle

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Introduction

Female infertility is responsible for approximately half of all cases of infertility and one of the causes of infertility in women is related to ovarian disorders. anti-mullerin hormone (AMH) is produced by the granulosa cells of pre-antral and small antral ovarian follicles and is widely accepted as a clinical marker of ovarian reserve (1). It is a member of the transforming growth factor-β superfamily, and there is a strong positive correlation between circulating AMH concentrations and the number of follicles in the ovary (2). Since the number of follicles is well correlated with the level of AMH (3), it can reflect the number of dormant follicles in adult women. AMH suppresses the cyclic recruitment of primordial follicles into the pool of growing follicles and its levels decrease with age (4,5), thus serving as a marker of female reproductive aging (6). AMH level is highly variable among women, even measured on the same day in the menstrual cycle. Serum AMH level has been reported to be a highly accurate tool for the diagnosis of polycystic ovary syndrome (PCOS) (7) and premature ovarian insufficiency (8). In addition, AMH is used for the prediction of ovarian response during in vitro fertilization (IVF) treatment, and prediction of age at menopause (9,10).

The fact that AMH can't predict the probability of a woman conceiving within a given period may be related partly to variation of circulating AMH even within the same age in different women (11) due to various lifestyle and reproductive characteristics. Konishi et al. (2014) examined the association between AMH levels and menstrual cycle and lifestyle characteristics among young Japanese women. They reported that circulating AMH concentration was significantly lower among young women who had more severe menstrual pain (12). Lower AMH concentration has been found in using oral contraceptives (13), mild/ minimal endometriosis (14), obesity (15), smoking (16), and a regular and shorter menstrual cycle (13).

Physical activity plays an important role in maintaining energy balance which may affect the reproductive system (17). Weight loss via physical activity may protect ovarian function by increasing insulin resistance and changing the hormonal profile (18). It has been reported that an increased risk of infertility was found for the group of women reporting the highest levels of intensity and frequency of physical activity (19). Thus the possible risks of infertility should be highlighted among women who do heavy exercise. Steiner et al. (2010) reported that serum AMH levels do not fluctuate during oral contraceptive use in reproductive-aged women and AMH levels are significantly lower in obese women (1). It has been reported among premenopausal women, that lower AMH levels are associated with older age, younger age at menarche, and currently using oral contraceptives, suggesting these factors are related to decreased ovarian follicles (20). Bernardi et al. (2017) reported a significant association between obesity and lower AMH levels, suggesting that obesity may compromise ovarian reserve(21) through decreased responses to fertility medications, fewer oocytes retrieved (22), and lower pregnancy and live birth rates (23). However, there are contradictions in the literature regarding the association between obesity and AMH levels, so further investigation into this relationship is warranted.

On the other hand, ethnicity is an independent predictor for AMH (18) and the association between AMH and lifestyle factors like body mass index (BMI), smoking, and physical activity may vary across ethnic groups (13). Understanding the factors associated with individual variation of AMH levels among infertile women may help their infertility management. To our knowledge, no study has targeted in North Iranian between infertile women to examine such associations. Therefore, the present study aimed to evaluate the association between age, BMI, reproductive history, and physical activity with serum AMH concentration in North Iranian women with primary/secondary infertility.

Materials and Methods

Subjects

This cross-sectional study included 234 women aged 18–45 from April 2019 to March 2020. Patients participating in the study were selected from women candidates for assisted reproductive treatment and referred to the Infertility Clinic of the Al-Zahra Hospital, Rasht, Iran. Exclusion criteria included menopause, cancer, underlying endocrine diseases, use

of hormonal drugs, diagnosis of PCOS based on Rotterdam criteria, any ovarian and uterine surgery, and endometriosis. Approval was obtained from the Research Deputy and Ethics Committee of Guilan University of Medical Sciences (Approval ID: IR.GUMS.REC.1398.375). All the participants signed a written informed consent before sample collection and acknowledged that they had been fully anonymized. The reproductive characteristics included age at menarche, cycle regularity status, pregnancy, parity, breastfeeding history, and age at menarche, maternal menopause age. The amount of physical activity of the patients was also recorded. IPAQ (International Physical Activity Questionnaire) (24) was used to determine the amount of physical activity.

AMH assay

At the time of enrollment up to 5 mL of venous blood was drawn from each participant. Blood samples were centrifuged at 1400g/10min to separate the serum. Serum samples were stored at -20 °C until AMH concentration measurement. Serum AMH was measured using the Beckman Coulter AMH ELISA kit (cat no: B13127) according to the manufacturer's instructions.

Statistical analysis

Statistical analyses were performed using SPSS Software (v21; SPSS Inc; Chicago, Illinois, USA), and P-values less than 0.05 were considered significant and Chi-square tests, fisher exact test, and independent T-test were used to examine the relationship between variables

Results

This cross-sectional analysis included 234 women aged 18–45 years old referred to the Infertility Clinic of the Al-Zahra Hospital, Rasht, Iran. Table 1 includes information on the demographics and reproductive history of the women who participated in the study. As expected, we observed significantly lower AMH concentrations in older participants. The risk of infertility is increased for the group of women who report the highest intensity and frequency of physical activity. There was no significant association between BMI and AMH concentrations (P= 0.37). There was no association between reproductive determinants and AMH level (Table 1).

Table 1. Demographic characteristics and reproductive history of two groups of study.

Variables	AMH≤1.10	AMH≥1.11	P value
Age (years)			
18-30	9(9.1%)	37(27.4%)	**0.0001***
30-40	37(37.4%)	85(63%)	
>40	53(53.3%)	13(9.6%)	
BMI (kg/m2)			
<25	33(33.3%)	42(31.1%)	**0.371***
25-30	44(44.4%)	52(38.5%)	
≥30	22(22.2%)	41(30.4%)	
Breastfeeding history			
No	90(90.9%)	120(88.9%)	**0.615***
Yes	9(9.1%)	15(11.1%)	
Menstrual cycle pattern			
Regular	75(75.8%)	96(71.1%)	**0.429***
Irregular	24(24.2%)	39(28.9%)	
Gravidity			
0	72(72.2%)	99(73.3%)	**0.918***
≥1	27(27.3%)	36(26.7%)	

Abortion			**0.115***
0	79(79.8%)	118(87.4%)	
≥1	20(20.2%)	17(12.6%)	
Live birth			**0.295***
0	92(92.9%)	120(88.9%)	
≥1	7(7.1%)	15(11.1%)	
Still birth			**0.700****
0	96(97%)	132(97.8%)	
≥1	3(3%)	3(2.2%)	
Age at menarche	12.86±1.31	12.93±1.33	**0.70*****
Maternal menopausal age	50.54±2.47	50.85±2.86	**0.93*****

*** Chi-squared test** **** fisher's exact test** ***** independent t-test**

Physical activity is classified into fourepresentsr groups vigorous physical activity, moderate physical activity, low physical activity (walking), and inactive (sitting). As shown in Figure 1, lack of physical activity, as well as vigorous physical activity, is associated with lower AMH concentration (P= 0.025, and P= 0.039 respectively).

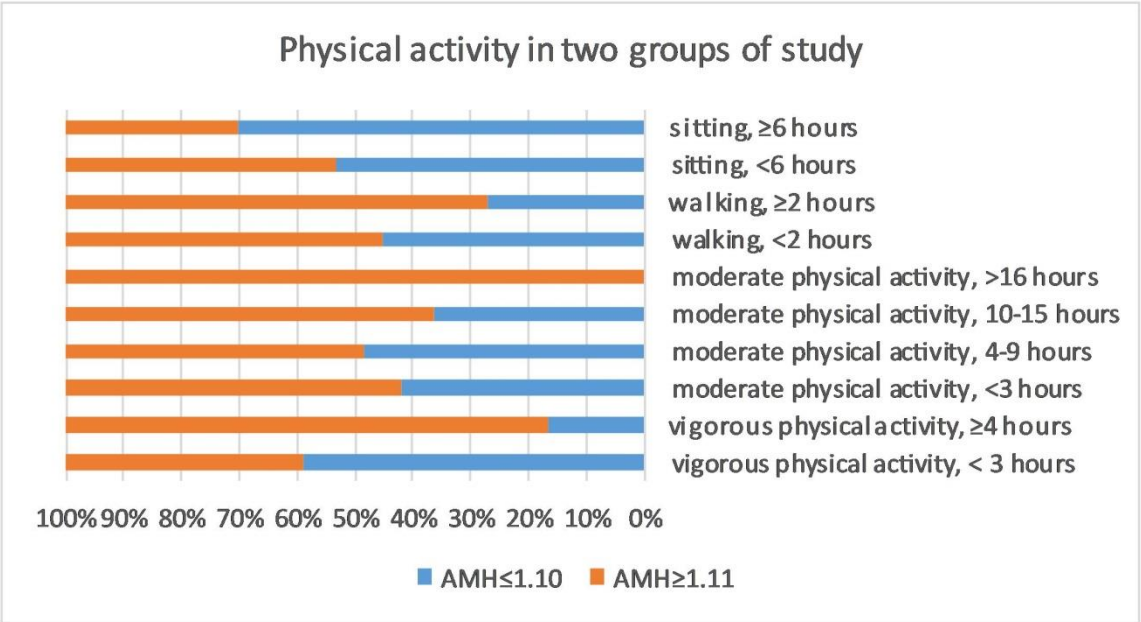

Figure 1. The chart representing physical activity in two groups of study. As shown in the chart, lack of physical activity as well as vigorous physical activity is associated with AMH ≤1.10.

Discussion

This study demonstrated that AMH levels are influenced by physical activity. More specifically, we found lack of physical activity, as well as vigorous physical activity, is associated with lower AMH concentration. Improvement of AMH levels and oxidative stress through regular exercise has been

reported in Chinese women with PCOS (25). So, improvement of oxidative stress might be an effective method for improvement of AMH level, which deserves further research. It has been reported that the level of AMH in women over 40 years of age was significantly lower than in women less than 35 years of age. Jung et al.(2017) reported higher AMH concentrations in women with older compared to younger ages at menarche (20) while our finding is consistent with other study reported no associations (26). We also observed no association between other reproductive determinants (Table 1) which may be due to the small sample size of the present study or ethnicity variations. So, future large studies are warranted to validate our findings. We observed no association between parity and AMH level that is consistent with earlier studies (20). The decrease of AMH levels with increasing age in adult premenopausal women is well established (26,27) as we observed in this present study.

Regular exercise causes weight loss and improves metabolic function and hormonal profile. It has been reported that the exercises also usually lead to a significant increase in fertility (28). Physical activity improves the quality of life in the general population but there is insufficient evidence for the effect of physical activity and quality of life on improving fertility in infertile women (29). Cicek et al. (2019) reported strength exercise decreases serum AMH levels and increases serum FSH levels (30). Therefore, excessive exercise practices have negative consequences for women's fertility, especially for those with lower ovarian reserve. It has been reported that moderate physical activity is associated with improved age-specific levels of ovarian reserve markers (31).

Physical activity through regulation of energy balance and insulin sensitivity can improve reproductive system function. Vigorous physical activity was associated with reduced fecundity in all women with normal BMI, but not in overweight and obese women (32). However, it has been demonstrated physical activity is unlikely to have a deleterious effect on IVF success and certain forms of vigorous activity may be beneficial (33). AMH can predict the ovarian response to hyperstimulation (34) and a low AMH test result has a negative psychological impact (35). On the other hand, maternal lifestyle during pregnancy may be associated with reproductive health and ovarian reserve in adult offspring (36). So, finding an association between lifestyle parameters such as physical activity and the level of AMH, and changing this lifestyle can affect the health of the next generation.

Conclusions

In this study, AMH levels appear to be significantly lower in patients with a lack of physical activity as well as vigorous physical activity. The results of the present study showed that by improving lifestyle, including the appropriate amount of physical activity, it may be possible to improve hormone levels and thus improve the results of infertility treatments. However, a larger clinical study is indicated to study the association between AMH and physical activity in reproductive-age women.

Author contribution

In this manuscript, the role of each of the authors, conceptualization with **RK**, conceptualization with **FM**, data collection with **ME**, formal Analysis with **AA**, writing, review and editing with **NGhG**, and writing an original draft with **SHSh**.

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Conflict of interest

The authors report no conflict of interest.

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