International Journal of Research in Medical Sciences
Farzipour S et al. Int J Res Med Sci. 2023 Oct;11(10):xxx-xxx
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms2023????

Original Research Article

Study serum anti-Mullerian hormone levels in women undergoing IVF and its association with affecting factors

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Received: 31 July 2023
Revised: 02 September 2023
Accepted: 04 September 2023

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ABSTRACT

Background: Infertility means inability of pregnancy after one year of natural continuous intercourse, not using any prevention which is one of the most important problems in every human society. The average rate of infertility in different societies is been estimated to be 8-12%. The aim of this study was to determine the level of anti-Mullerian hormone (AMH) in women undergoing IVF and its associations with effective factors.
Methods: This was a cross-sectional study which was done by using library and field methods. A number of 170 women with the diagnosis of infertility referring to the infertility clinic of Alavi hospital in Ardabil city from August 2021 to December 2021 were enrolled randomly in the study and their clinical data including demographic, anthropometric and hormone levels were gathered and then analyzed by using statistical methods in SPSS version 22 software.
Results: The mean age of women were 31.7±4.68 and AMH level were 3.35±2 ng/ml. There was a strong association between age and AMH level (r=0.68, p=0.001). There was not a significant correlation BMI and AMH levels. In women with the complaint of secondary infertility, prevalence of AMH deficiency was significantly lower than other women (p=0.045). There was no difference in AMH levels between regular and irregular monthly menses.
Conclusions: It can be concluded from our study that increase of age is one of the main factors in AMH levels. Also, the deficiency of this hormone can be a cause in secondary infertility.

Keywords: Anti-Mullerian Hormone, Infertility, Pregnancy

INTRODUCTION

Fertility means the ability of the reproductive system to conceive and maintain it until the right time for delivery. Female fertility is declining with age and the loss of previous pregnancies. Simultaneously with reduced fertility woman's ovarian quality and storage also decline. One of the criteria for determining the quality of an ovulation is the number of its chromosomes or the so called "ploidy" related it.[1]

Infertility, is the inability to conceive after one year of natural, continuous and unprotected intercourse, which is one of the most important health problems in all human societies. The average prevalence of infertility in different communities is estimated at 8% to 12%. The causes of infertility are numerous. Some of them are physiological and various factors such as genetic disorders are involved in their occurrence, but many environmental and acquired factors also affect fertility and can cause infertility.[2] For example, increasing age plays a major role in reducing fertility and complications during pregnancy. A study in Sweden found that fertility rates dropped by 3.5 % each year after the age of 30 and 30 percent of couples whose wives are aged 35-44 are infertile.[2,3]

Ovarian reserve is the number of mature and healthy oocytes in the ovary that clearly decreases with age.[3] This decrease is so great that the total number of follicles

reaches approximately twenty five thousand follicles in a woman aged 37-38 years (of 300,000 follicles under the age of 35) and this decrease is associated with increasing FSH and decreasing Inhibin. These changes are due to a decrease in the quality and capacity of older follicles.[4]

FSH, inhibin B, estradiol, number of antral follicles and ovarian volume are better methods for estimating ovarian storage.[4] Ovarian storage markers, including ultrasound modalities and serum markers, have been well studied in people with infertility problems in recent years and it seems to be important to identify a serum marker that is, on the one hand, a reflection of the number of follicles passing from the primitive to the growing state and on the other hand, independent of gonadotropin control, it is likely to be a reliable measure of quantitative ovarian storages. One of these potential markers is anti-Mullerian hormone. In recent years, serum levels of anti-Mullerian hormone (AMH) have been shown to be a good option for estimating ovarian reserve. AMH is a member of the transforming growth factor beta (TGF β) superfamily, which is expressed in Sertoli cells of the male's reproductive system during embryonic development. In women after birth, anti-Mullerian hormone is produced in large quantities by granulosa cells in the preantral and antral follicles and secreted into the bloodstream. A slight increase in ovarian life is characterized by a decrease in the storage of primitive follicles.[5,6] Therefore, this hormone as a factor that is initially secreted by the growing follicles is a reflection of the amount of storage of primitive follicles. A study has shown that AMH can well indicate the potential for ovarian potential efficiency in artificial stimulation.[7] Direct measurement of this reserve is impossible but can be indirectly assessed by counting the number of growing follicles. Studies have shown that there is a positive relationship between ovarian follicular storage and serum AMH levels, which gradually, with the development of follicles, the secretion of AMH decreased.[6]

The aim of this study was to evaluate the level of AMH in IVF infertility patients and the factors affecting it.

METHODS

This was a cross-sectional study was performed on 170 patients who referred to the infertility center of Alavi hospital in Ardabil city from August 2021 to December 2021. AMH levels were measured by ELISA in these patients before starting the treatment. Other factors involved in AMH were extracted from the patient's history and medical records and recorded in a checklist. Women with comorbidities including blood diseases with a history of recent chemotherapy, PCO, history of ovarian surgery, patients with severe vitamin D deficiency, OCP users and those with BRCA1 mutation that effect the level of AMH were excluded from the study.

Collected data were entered into SPSS version 22 and analyzed by using descriptive statistics in the form of tables and graphs. We also used statistical methods using t-test and chi-square for determine the relation between quantitative and qualitative data. The p value less than 0.05 was considered significant. The present study was approved in the ethics committee of Ardabil University of Medical Sciences and registered with the code IR.ARUMS.REC.1399.144.

RESULTS

The average age of all women was 31.7±4.68 years. There was a significant difference between AMH and infertile period in age groups (Table 1).

Table 1: Values of body mass index, AMH and length of infertility period by age group.

	20-25	26-30	31-35	36-40	>40	P value
AMH	4.72±1.91	3.63±1.33	2.72±1.52	1.78±1.09	1.02±0.82	0.001
BMI	26.19±5.35	27.23±4.91	28.21±5.14	28.61±6.2	27.55±3.83	0.079
Infertility period	2.11±1.8	3.1±2.1	4.8±2.6	5.9±3.1	6.2±4.3	0.001

There was a strong correlation between age and AMH levels, (p=0.001, r=0.68) (Figure 1).

AMH levels decreased with increasing body mass index, but this relationship was not statistically significant (Figure 2).

To eliminate the effect of age, AMH data were adjusted based on the age of patients and were divided into two categories: patients with AMH deficiency and patients without AMH deficiency. Comparison of these two groups showed that in women with secondary infertility complaints, the prevalence of cases of AMH deficiency was significantly more than other women (p=0.045) (Table 2).

Comparison of these two AMH groups showed that there was no difference in AMH levels in women with regular and irregular menstruation based on age groups (Table 3).

Finally, the relationship between AMH level and the duration of the infertility period was measured, results showed that with increasing the duration of the infertility period, the AMH level decreases (p=0.013, r=0.189) (Figure 3).

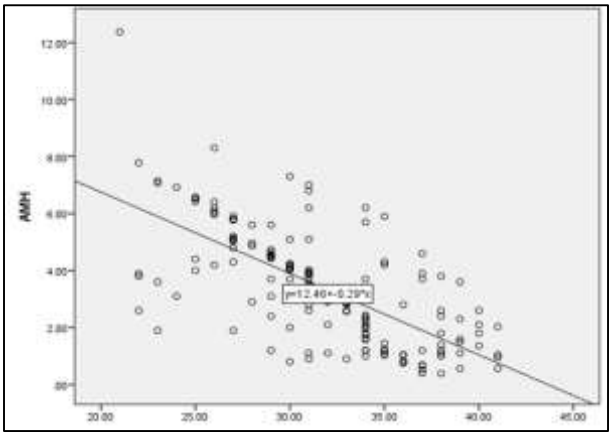

Figure 1: Relationship between serum AMH level and age.

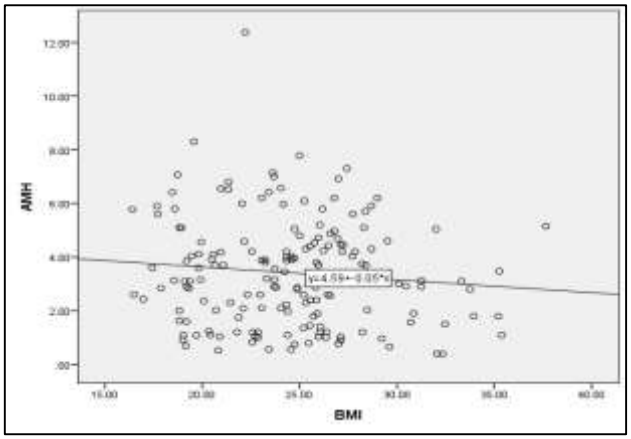

Figure 2: Relationship between body mass index and serum AMH level.

Table 2: Frequency distribution of AMH values and type of infertility by age group.

Age groups (years)	Infertility		AMH		P value
			Deficiency	Without deficiency	
20-25	Primitive	N	1	14	0.413
		%	100	87.5	
	Secondary	N	0	2	
		%	0	12.5	
26-30	Primitive	N	7	28	0.217
		%	63.6	71.8	
	Secondary	N	4	11	
		%	36.4	28.2	
31-35	Primitive	N	4	31	0.449
		%	50	58.5	
	Secondary	N	4	22	
		%	50	41.5	
36-40	Primitive	N	2	8	0.891
		%	33.3	32	
	Secondary	N	4	17	
		%	66.7	68	
>40	Primitive	N	3	3	0.328
		%	50	60	
	Secondary	N	3	2	
		%	50	40	

*The criteria for AMH deficiency in the ages of 20-25, 30-26, 35-31, 40-36 and over 40 years are 1.5, 1, 0.75, 0.3 and 0.1; respectively.

Table 3: Relationship between AMH level and menstrual cycle.

Age groups (years)	Menstrual order		AMH		P value
			Deficiency	Without deficiency	
20-25	Regular	N	0	12	0.426
		%	0	85.7	
	Irregular	N	1	2	
		%	100	14.3	
26-30	Regular	N	5	19	0.472
		%	50	59.4	
	Irregular	N	5	13	
		%	50	40.6	

Continued.

Age groups (years)	Menstrual order		AMH		P value
			Deficiency	Without deficiency	
31-35	Regular	N	4	26	0.892
		%	57.1	57.8	
	Irregular	N	3	19	
		%	42.9	42.2	
36-40	Regular	N	2	14	0.0019
		%	33.3	60.9	
	Irregular	N	4	9	
		%	66.7	39.1	
>40	Regular	N	2	1	0.111
		%	33.3	0.25	
	Irregular	N	4	3	
		%	66.7	0.75	

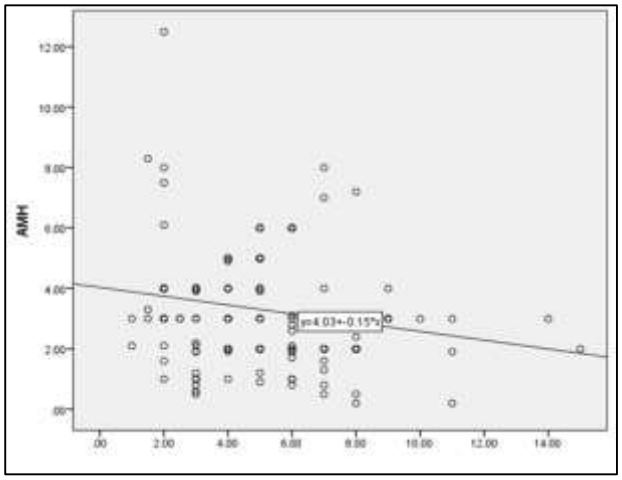

Figure 3: Relationship between infertility length and serum AMH level.

DISCUSSION

In a 2012 study by Erfanian et al, the average age of women with infertility complaints who underwent IVF was 35.6 5.16, 16 years and the average age of these women did not differ significantly based on serum AMH levels.[8] In a 2015 study by Aydin et al, the average age was 32.1 years and it was found that the average AMH in older women was significantly lower than younger women.[9] Most studies have reported an inverse relationship between body mass index and AMH levels. A 2011 study by Buyuk et al, found that there was an inverse relationship between body mass index and AMH serum levels in women with decreased ovarian storage.[10] A 2015 study by Iwase et al, also found an inverse relationship between serum AMH levels and body mass index in patients with polycystic ovaries.[11] Studies by Freeman et al in 2007 and Su et al in 2008 also reported an inverse relationship between serum AMH levels and body mass index.[12,13] Some studies have shown that there is no significant relationship between these two indicators. For example, studies by Halawaty, Simões-Pereira and La Marca have reported unrelated serum AMH and body mass index.[14-16] Contrary to the findings of the above studies, in a study conducted by Albu et al, in 2019, a positive correlation was found between AMH values and body mass index in infertile women after adjusting the data in term of age, which is a unique result and according to research the only study that has been done with this conclusion.[17] In the present study, no correlation was reported between body mass index and serum AMH levels, which is in line with the studies mentioned earlier. This result is important because it can be considered to refuse the hypothesis of improving AMH index by weight loss in patients with overweight or obesity, which requires future interventional studies to prove this hypothesis. Supplementary studies in the present study showed an inverse relationship between the duration of infertility and serum AMH levels. The duration of infertility in many cases is a function of the age of the patients. Therefore, it is expected that the same inverse relationship will be established between the duration of infertility and serum AMH levels. This claim is also accepted in a study by Hehenkamp.[18] Another indicator studied in the evaluation of AMH and reproductive health was the order and duration of menstrual cycles. In a study by Marsh et al, a positive correlation was found between AMH levels and menstrual cycles of more than 35 days.[19] In a study by Dolleman et al, which examined the effect of lifestyle on women's sexual status, it was found that the average AMH percentile in women with irregular menstruation was significantly lower than other women.[20] However, in the present study, although the average serum AMH level in women with irregular menstruation was lower than other women, however, this difference was not statistically significant, which may be due to the low sample size due to incomplete file of patients. Also, due to inter-racial and inter-population differences, compiling AMH percentiles in the population of Iran and the Middle East can provide a more accurate index of normal and abnormal forms in patients in this region. A study by Benksim et al, in Morocco found that hormonal disorders (including AMH, LH, and FSH) were significantly lower

in patients with secondary infertility than in women with primary infertility; however, in this study, AMH was not specifically addressed and all sex hormones were examined in one spectrum.[21] It is also clear that in many cases, the age of women with secondary infertility is higher than women with primary infertility that this age difference can affect serum AMH levels. In the present study, to eliminate the effect of age, AMH data were adjusted based on the age of patients and classified into two groups: patients with AMH deficiency and patients without AMH deficiency. Comparison of these two groups with each other showed that in women with secondary infertility complaints, the prevalence of cases of AMH deficiency is small but significantly higher than other women.

One of the main limitations of the present study is the lack of similar studies, especially in Iran and the region to compare results. The incompleteness of many files also made data collection difficult.

CONCLUSION

Finally, from the present study, it can be concluded that aging is one of the main factors reducing serum AMH. Also, deficiency of this hormone can also be considered a cause of secondary infertility. Increasing body mass index has no effect on decreasing AMH levels and menstrual cycle has no effect on AMH levels.

Recommendations

Finally, it is suggested that a study with a similar subject and a larger sample size be conducted in this region. Also, localizing benchmark data such as AMH percentile charts can be helpful in future. It is hoped that the results of this study will be a positive step in the field of diagnosis, treatment and prevention in these patients.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee and registered with the code IR.ARUMS.REC.1399.144

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Cite this article as: Farzipour S, Jalilvand F, Shojaei SS. Study serum anti-Mullerian hormone levels in women undergoing IVF and its association with affecting factors. Int J Res Med Sci 2023;11:xxx-xx.