The relationship between anti mullerian hormone level and endometrial polyp frequency in patients with polycystic ovary syndrome

Polikistik over sendromlu hastalarda anti müllerian hormon düzeyi ile endometrial polip sıklığı arasındaki ilişki

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ABSTRACT

Aim: This study aimed to conduct a case-control study to determine the relationship between serum anti mullerian hormone (AMH) levels and frequency of endometrial polyp in women with polycystic ovary syndrome (PCOS).

Material and Method: Patients with endometrial polyps (n=55) were included in the study group. The control group was selected from women without endometrial polyps (n=49). The relationship between the case and control groups was studied using the chi-square test to check the AMH levels and endometrial polyps.

Results: The participants' age and body mass index (BMI) were 28.20±3.08 and 25.45±2.25, respectively. There was a statistically significant association between AMH levels and endometrial polyp (p-value <0.001). There was no significant difference between the endometrial polyps group and the control group in terms of age, BMI, prolactin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), dehydroepiandrosterone sulphate (DHEA-SO4), total testosterone, estradiol, thyroid-stimulating hormone (TSH) and thyroxine (T4) (p-value >0.05).

Conclusion: This research showed that the frequency of endometrial polyps increases with higher AMH levels in PCOS patients.

Keywords: Anti mullerian hormone, endometrial polyp, polycystic ovary syndrome

ÖZ

Amaç: Bu çalışmada polikistik over sendromlu (PKOS) kadınlarda serum anti mullerian hormon (AMH) düzeyleri ile endometrial polip sıklığı arasındaki ilişkiyi belirlemeyi amaçladık.

Gereç ve Yöntem: Çalışma grubuna endometrial polipli hastalar (n=55) dahil edildi. Kontrol grubu endometrial polip olmayan kadınlardan (n=49) seçildi. Olgu ve kontrol grupları arasındaki ilişki, AMH düzeylerini ve endometriyal polipleri kontrol etmek için ki-kare testi kullanılarak araştırıldı.

Bulgular: Katılımcıların yaş ve vücut kitle indeksi (VKİ) sırasıyla 28,20±3,08 ve 25,45±2,25 idi. AMH seviyeleri ile endometrial polip arasında istatistiksel olarak anlamlı bir ilişki saptandı (p değeri <0,001). Endometriyal polip grubu ile kontrol grubu arasında yaş, VKI, prolaktin, folikül uyarıcı hormon (FSH), luteinize edici hormon (LH), dehidroepiandrosteron sülfat (DHEA-SO4), total testosteron, östradiol, tiroid uyarıcı hormon (TSH) ve tiroksin (T4) değerleri açısından anlamlı farklılık saptanmadı (p değeri >0,05).

Sonuç: Bu araştırma, PKOS hastalarında yüksek AMH seviyeleri ile endometrial polip sıklığının arttığını göstermiştir.

Anahtar Kelimeler: Anti müllerian hormone, endometrial polip, polikistik over sendromu

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women, which is manifested in 5-8% of women of reproductive age and is one of the most important causes of infertility (1). Chronic anovulation and clinical or laboratory signs of hyperandrogenism are symptoms of PCOS (2). Among the subcriteria for diagnosing this syndrome are insulin resistance, the onset of obesity and premenarche hirsutism, the luteinizing hormone (LH) to follicle-stimulating hormone (FSH) ratio above, and sonography evidence of PCOS (3).

One of the causes contributing to the diagnosis of this disease is anti mullerian hormone (AMH) (4). AMH is a member of the large TGF_B beta factor family, secreted by the granulosa cells of small follicles to regulate the initial stages of follicle growth. AMH is used to predict and determine ovarian reserve and the quality of remaining oocytes (5,6).

AMH is a hormone produced by the growing follicles (containing ovum). For this reason, it is regarded as an indicator of the number and quality of ovum produced in the menstrual cycle. Few studies have been conducted on the relationship between serum levels and the incidence of endometrial polyps in PCOS women (7). Excessive growth of cells in the endometrial inner lining leads to the formation of uterine polyps, which are also called endometrial polyps. The incidence of endometrial polyps in infertile women of reproductive age is about 15% (8).

Endometrial polyps play an important role in infertility, implantation failure and recurrent miscarriages (9). Uterine polyps prevent the transfer of sperm, and for this reason, they have a direct effect on the pregnancy trend. Identification of markers in the manifestation of endometrial polyps plays a vital role in providing diagnosis and effective treatment methods.

Considering the complications caused by PCOS disease and the heavy economic burden of this disease for treatment of infertility, the lost years of life and its mental burden on the family, and the lack of sufficient information in this field in the country, one should conduct the study of the relationship between AMH serum level as a diagnostic marker of the probability of uterine polyps among the PCOS women.

This study aimed to conduct a case-control study to determine the relationship between AMH serum level and endometrial polyps in PCOS women to give the results for future actions in this field.

MATERIAL AND METHOD

This study was started after the ethical approval of the study was obtained from Beykoz University Clinical Researches Ethics Committee (Date: 21.01.2021, Decision No: 2). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This retrospective study evaluated patients who had endometrial polyps at Medistate Hospital Gynecology and Obstetrics clinic between January 2019 and December 2020.

Patients with endometrial polyps (n=55) were included in the study group. The control group was selected from women without endometrial polyps (n=49). All the participants had PCOS disease. Endometrial polyps were detected by ultrasound. According to 2003 Rotterdam consensus, the criteria for the diagnosis of PCOS are having two of the following: 1) oligoovulation, 2) hyperandrogenism and 3) polycystic ovaries (≥ 12 follicles measuring 2-9 mm in diameter and/or an ovarian volume > 10 mL in at least one ovary).

Information about the serum AMH levels were collected from medical records. AMH enzyme immunoassay (Instrumentation Laboratory and Beckman-Coulter, Vienna, Austria) was used to specify serum AMH (ng/ml).

The inclusion criteria were: (1) the woman between the ages of 20 and 45. The exclusion criteria were: (1) pregnant women and women in the breastfeeding period; (2) absence of diabetes, thyroid dysfunction, and systemic diseases.

Statistical Analysis

The Kolmogorov-Smirnov test was performed to check the normality, and the nonparametric tests were performed given the non-normality of the groups before the statistical analyses. Mean and standard deviations (SD) were measured to check each continuous variable, including age, body mass index (BMI), infertility period, AMH, FSH, LH, Prolactin, dehydroepiandrosterone sulphate (DHEA-SO4), total testosterone, estradiol, thyroid-stimulating hormone (TSH) and thyroxine (T4) . The relationship between the AMH levels and endometrial polyps was compared using the chi-square test. The Mann-Whitney test is performed to study the difference between the two groups. SPSS v20 was used for statistical analyses. A value of p-value < 0.05 was accepted as statistically significant.

RESULTS

The study included 104 women (mean age±SD: 28.20±3.08). The participants' BMI were 25.45±2.25. **Table 1** shows descriptive statistics of study parameters. **Table 2** shows the relationship between AMH level and endometrial polyp.

Table 1. Descriptive statistics of study parameters in women (n=104).

Study parameters	median (range)	mean±SD
Patients characteristics		
Age	28 (22-36)	28.2±3.08
BMI	25 (20-33)	25.45±2.26
Infertility Period(years)	3 (0-5)	3±1.35
Laboratory values		
AMH (ng/ml)	5.8 (2.3-14.5)	6.22±2.57
FSH	5.68 (1.79-9.66)	5.65±1.81
LH	6.14 (2.73-22.8)	7.48±4.32
Prolactin	20.41 (2.57-143)	26.53±20.33
TSH	2.48 (0.46-7.98)	2.71±1.42
T4	1.24 (0.95-2.75)	1.27±0.26
DHEA-SO4	265.15 (33.8-671)	288.92±118.07
Total testosterone	32.5 (3-141)	37.05±22.7
Estradiol	50.02 (6.98-330.9)	70.56±60.95

SD, standard deviation.

Table 2. The relationship between AMH level and endometrial polyp

Variable level	Endometrial Polyps (n=55) n (%)	No Endometrial Polyps (n=49) n (%)	p
AMH levels			<0.001*
AMH≤5	†10 (18.20)	24 (49)	
5<AMH <7	21(38.20)	17 (34.7)	
AMH≥ 7	24(43.60)	†8 (16.3)	

*A chi-square test † Pairwise Z-Tests

As stated in Table 2, a chi-square test found a statistically significant association between AMH levels and endometrial polyp (p-value < 0.05). Data in **Table 1** are presented as numbers (percentages). The number of polyps increases with the increase of AMH. The prevalence of endometrial polyp in women with AMH≤5 was (18.20%), 5<AMH<7 (38.20%), and AMH≥7 (43.60%). **Figure** shows the frequency of endometrial polyps at different AMH levels.
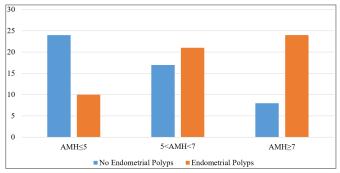

Figure. Frequency of endometrial polyps in different AMH levels

The Pairwise Z-Tests found that the percentage of women who had the endometrial polyps was significantly higher for those who had AMH < 5 ng/ml than for those who had AMH > 5 ng/ml. Also AMH > 7 ng/ml decreased the endometrial polyps risk.

Table 3 shows the hormonal characteristics of the study groups. There was not a statistically significant difference between endometrial polyps group and control in terms of age (p=0.063), BMI (p=0.819), infertility period (p=0.136), FSH (p=0.749), LH (p=0.686), prolaktin (p=0.076), TSH (p=0.525), T4 (p=0.062).DHEASO4 (p=0.212), total testosterone (p=0.564), and Estradiol (p=0.297).

There was a statistically significant difference between endometrial polyps group and control in terms of AMH levels (p < 0.05).

Table 3. Average of study parameters according to the endometrial polyps result

Study parameters	Endometrial Polyps (n=55)	Mean±SD	No Endometrial Polyps (n=49)	Mean±SD	p
Age (years)	29(22-36)	28.91±3.41	27(22-32)	27.41±2.47	0.063*
BMI	25(20-33)	25.6±2.7	25(22-29)	25.29±1.63	0.819*
Infertility Period(years)	3(0-5)	2.78±1.42	3(1-5)	3.24±1.23	0.136*
AMH (ng/ml)	6.5(3.2-14.5)	7.16±2.63	5.1(2.3-11)	5.17±2.05	<0.001*
FSH	5.76(1.79-9.66)	5.71±1.87	5.66(2.4-9.51)	5.59±1.74	0.749**
LH	6.32(2.73-22.8)	7.63±4.61	5.8(2.73-19.36)	7.31±4.01	0.686*
Prolactin	22.59(5.08-143)	32.33±25.14	18.45(2.57-46.73)	20.03±9.7	0.076*
TSH	2.42(0.46-7.98)	2.71±1.58	2.57(0.54-6.7)	2.7±1.24	0.525*
T4	1.21(0.95-2.75)	1.24±0.26	1.28(0.95-2.75)	1.31±0.27	0.062*
DHEA-SO4	268.7(125.7-671)	306.81±129.29	262.8(33.8-545.6)	268.84±101.65	0.212*
Total testosterone	32(3-141)	36.8±25.54	34(5-84)	37.34±19.27	0.564*
Estradiol	47.12(21-330.9)	68.76±63.82	55(6.98-275.6)	72.58±58.17	0.297*

* Mann-Whitney test **The independent t-test, BMI, body mass index ; AMH, anti-Mullerian hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone; T4, Thyroxine; DHEA-SO4, dehydroepiandrosterone sulphate.

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DISCUSSION

This study aimed to conduct a case-control study to determine the relationship between AMH serum levels and endometrial polyps in women with PCOS. AMH is helpful in evaluating women at risk of decreased ovarian reserve, including women with a family history of ovarian failure (10), women with early menopause (11), women with a history of severe endometriosis (12), chemotherapy or previous surgery on the ovaries (13), women with autoimmune diseases (14), pelvic infections (15), and women using vegetarian diets (16).

This retrospective study showed that in women with PCOS, the endometrial polyps increase the level of AMH levels. In various studies, the relationship between AMH and PCOS has been discussed. It has been shown that androgens cause the proliferation of the inner theca and granulosa layer, which can increase AMH (10-16). Also, the level of AMH can be highly related to the number of antral follicles and oocytes (17). Therefore, there is an increase in the serum level of AMH in PCOS patients with endometrial polyps (14,17,18).

Although the serum AMH level cannot accurately predict the risk level of endometrial polyps in women with PCOS, different studies have found different threshold levels (from AMH 3.8 to 5 ng/cc) to be sensitive for diagnosis (16,19,20). In a study conducted by Munro (20) on 60 PCOS cases and a control group, there was a significant difference in the average AMH level in patients with 14.7 and 3.14 in the control group. In another study, it was concluded that androgens could increase AMH (20). But the important thing to note in this study was the investigation of other factors that could affect the AMH level. Our study argued that the level of AMH is higher in PCOS women with endometrial polyps than in the control group, independently of other factors such as androgens and testosterone.

In the current study, the average AMH in the endometrial polyp group was 7.16 and in the control group was 5.17. The difference in hormone levels between the two groups was significant with $p > 0.001$, which shows a significant difference in the AMH level of the two groups. Other studies have concluded that AMH and PCOS can be a good differentiator between endometrial polyp sufferers and non-affected people (16,19). As in this research, a clear difference was seen between the level of this hormone in endometrial polyp and healthy subjects. Zhang et al. (21) studied 104 women with PCOS and found no relationship between AMH and BMI in patients, which is consistent with the findings of our study.

Considering that the patients' race in this study differs from other studies, there will be expected differences in the obtained results. The difference in the level of AMH, along with the difference in LH level and the ratio of LH to FSH in patients, can help in the early diagnosis of the disease (22,23). An important point is the low average age of patients without endometrial polyps in this study. As a result, it is possible to reduce the burden of the disease in the early stages of infertility by correctly diagnosing and treating it. Despite extensive and growing research in the field of PCOS and AMH, unfortunately, very few studies have been conducted on the effect of other factors, including endometrial polyps, on AMH in PCOS sufferers.

The study's retrospective nature and the subsequent lack of data due to file reading and the low accuracy of paraclinical results are the limitations of this study. Prospective studies and high measurement accuracy can help solve this limitation for future research.

CONCLUSION

This research, by examining AMH in two groups with endometrial polyps and non-endometrial polyps, showed that the frequency of endometrial polyps increases with higher AMH levels in PCOS patients and this result can be a platform for future research. Due to the study's retrospective nature and the impossibility of a detailed investigation of the effects of various other factors, a prospective study is recommended for future studies.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Beykoz University Ethics Committee (Date: 21.01.2021, Decision No:2).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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