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Original Article

The effects of anti-mullerian hormone, antral follicle count, and follicle stimulating hormone values on pregnancy outcomes in cases with polycystic ovary syndrome

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ABSTRACT

Objective: In this study, it was aimed to predict pregnancy by anti-mullerian hormone, follicle-stimulating hormone, and antral follicle count values of infertile patients with PCOS.

Methods: This retrospective study has been conducted on 555 patients diagnosed with PCOS (polycystic ovary syndrome) according to the Rotterdam Criteria, referred for infertility in the IVF Clinic of Istanbul Training and Research Hospital in the 2010-2019 study. Clinical pregnancy results have been analyzed together with anti-mullerian hormone, antral follicle count, and follicle-stimulating hormone levels.

Results: The age of the patients within the group of clinical pregnancy is significantly higher than the group without pregnancy ($p < 0.05$). Follicle-stimulating hormone (iu/ml) and anti-mullerian hormone (ng/ml) values do not differ significantly (p 0.05) in the group with and without clinical pregnancy. For the group with clinical pregnancy, the antral follicle count value is found to be significantly higher ($p < 0.05$) than the group without pregnancy.

The age of the patients in the group with clinical pregnancy was found to be significantly higher than the group without pregnancy. ($p < 0.05$). Follicle stimulating hormone (iu/ml) and anti-müllerian hormone (ng/ml) values did not differ significantly in the group with and without clinical pregnancy (p 0.05). Antral follicle count value was found to be significantly higher in the group with clinical pregnancy than in the group with out pregnancy ($p < 0.05$).

Although AFC was found to be significantly higher in the group with clinical pregnancy than in the non-pregnant group, it was examined diagnostically by ROC analysis, but the diagnostic capacity of this variable to distinguish between pregnant and non-pregnant women was not found to be sufficient. (AUC<0.70).

Conclusion: We found that anti-mullerian hormone and follicle-stimulating hormone are not related to clinical pregnancy outcomes in the infertile patient group diagnosed with PCOS (polycystic ovary syndrome). Plus, although the AFC value in the group with pregnancy was significantly higher than the group without pregnancy, its diagnostic capacity was not found to be sufficient.

Keywords: infertility; pregnancy; anti-mullerian hormone; AFC; polycystic ovary syndrome

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Introduction

Polycystic Ovary Syndrome (PCOS) is a chronic endocrine disorder with a prevalence of 5-10%. It is most commonly seen in women of reproductive age, and can occur in different periods of life due to the disruptions in the interactions between the central nervous system, pituitary, ovaries, and adrenal glands [1]. The prevalence of PCOS (polycystic ovary syndrome) can be determined according to the diagnostic criteria which are used [2,3]. Women diagnosed with PCOS are under the risk of dysfunctional bleeding, infertility, obesity, endometrial cancer, Type 2 Diabetes Mellitus (Type 2 DM), dyslipidemia, hypertension. Moreover, the risk of coronary artery disease is higher than the normal population.'Rotterdam Criteria' suggested by international consensus group (ESHRE)/(ASRM) is the gold standard for diagnosing PCOS, and a woman is diagnosed as PCOS if two out of the three following criterias are present: (1)Oligo/Anovulation, (2) Hyperandrogenism, which can be clinically and biochemically proved, (3) polycystic ovarian morphology (on ultrasound with a cut-off of more than 12 follicles with a diameter of 2–9 mm/when ovarian volume is more than 10 ml) [4].

Clinical symptoms of PCOS start with menarche, since the clinical course of the disease is affected by many different mechanisms, it varies periodically. While menstrual irregularities are generally seen at early ages, hirsutism and infertility occurs mostly in elderly patients [5,6]. The most common symptom of patients with PCOS in the reproductive period is menstrual irregularities starting from the peripubertal period. In the PCOS group, the first menstrual age is not delayed, but the following first periods are usually irregular. Anovulation in PCOS is a condition that begins in adolescence and appears as oligo or amenorrhea. Oligomenorrhea and amenorrhea can be detected in approximately 50% of the patients with PCOS [7]. PCOS is the most common cause for infertility in women of reproductive age [8,9]. An average of 70-85% of women with anovulation who wish to have children has PCOS. Ovulation abnormalities cause infertility in women with PCOS, while other factors, including metabolic morbidities, obesity and hyperandrogenism increase even more of this problem [10].

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In vitro fertilization (IVF) is an option that is recommended for infertility with no response to medical treatment in PCOS [11]. Antimullerian hormone (AMH) also termed müllerian inhibiting substance, is a member of the TGF-beta family and secreted by the granulosa cells of small antral (<8 mm) and pre-antral follicles to regulate early follicular development [12]. The AMH expression continues until follicles reach approximately 8 mm in diameter, and expression is insufficient in larger antral follicles. Consequently, there is a good correlation between antral follicle count (AFC) and AMH. The serum AMH concentration indicates the ovarian follicle pool containing antral follicles in the early follicular phase of the menstrual cycle. Therefore, a low AFC may result in low serum AMH levels [13,14]. The AMH level is accepted to be a reliable, direct indicator of decreased ovarian function. In patients of IVF, AMH level correlates with the number of oocytes retrieved after stimulation and is the reliable biomarker for predicting poor and excessive ovarian response [15]. AMH is significantly lower in patients with premature ovarian failure and controversy significantly higher in patients affected by PCOS [16]. The Antral Follicle Count (AFC) is considered a basic, reliable non-invasive method for determining the ovarian reserve. The number of antral follicles has become more predictive than basal Follicle Stimulane Hormone (FSH) and age, widely used in the evaluation of ovarian response and stimulation [17]. The hypothesis of this study assumed that the effect of PCOS patients on clinical pregnancy success may vary according to AMH, FSH VE AFC levels. This study aimed to investigate the effects of AMH, FSH, and AFC levels on pregnancy and assisted reproductive techniques outcomes in patients with PCOS. In our study, we aim to examine the ability of MPV, PCT, PDW, LMR, NLR, and CA 125, which are considered to play critical roles in the inflammatory process, to predict the stage of endometriosis.

Material and methods

This retrospective study is conducted on 555 PCOS patients diagnosed according to the Rotterdam Criteria who were referred to the IVF Clinic of Istanbul Training and Research Hospital for infertility between the years of 2010 and 2019. The study protocol was approved by the Ethics Committee of Istanbul Education and Research Hospital (Date: 09/08/2019Number: 1927) During the treatment process, the demographic data, applied artificial reproductive technique and clinical information of the patients are obtained from the patient files, and hospital database. Patients diagnosed with PCOS according to the Rotterdam criteria were included to this study. Exclusion criteria occur as follows: A history of ovarian surgery, ovarian cyst or tumor, hydrosalpinx, endometriosis, and endocrine or systemic diseases. In the study the AMH, FSH and AFC values of the patients diagnosed with PCOS according to Rotterdam criteria and their relation with clinical pregnancy rates have been examined. AFC were evaluated and reported by a gynecologist with transvaginal ultrasound on day 2nd-4th day of the menstrual cycle. Also FSH, AMH measurements were made on ultrasound examination days.

Statistical analysis

In the descriptive statistics of the data, mean and standard deviation, median and lowest, highest values used according to the normality tests. Categoric datas were presented as frequency and ratio. Mann-Whitney test and student t test used for the analysis of quantitative independent data, and the Chi-Square test is used for the analysis of qualitative independent data. SPSS 26.0 program is used for the analyses.

Results

This study is conducted on 555 patients with PCOS who were diagnosed according to Rotterdam Criteria and were referred to Istanbul Training and Research Hospital IVF Clinic for infertility between 2010 and 2019. For the classification of the collected data, assisted reproductive techniques applied to patients are taken into consideration, and the outcome treatment of patients who underwent more than one technique is included in the data.

The age of the cases was minimum 22 and maximum 46, with a median of 27. Treatment was planed for 30.1 percent of patients; IVF was applied to 22.9%,only ovulation induction to 3.8%, and the IUI protocol with gonadotropin to 3.4%. Spontaneous pregnancy was observed for approximately 9.2% of the patients without any treatment. (Table 1)

Table 1. Demographic data of patients

		Pregnancy negative	Pregnancy positive	Total
Treatment	None	337 (92,6)	51 (26,7)	388 (69,9)
	IVF	25 (6,9)	102 (53,4)	127 (22,9)
	IUI+OI	2 (,5)	38 (19,9)	40 (7,2)

Chi-square analysis was used by combining IUI and ovulation induction group treatments, and a significant difference was found between the three groups. Significance was found between those who did not receive any treatment and those who received IVF or IUI+IOI as treatment via Bonferroni correction. ($p<0.001$). The age of the patients within the group of clinical pregnancy is significantly higher than the group without pregnancy ($p < 0.05$). FSH and AMH values do not differ significantly (p 0.05) in the group with and without clinical pregnancy. For the group with clinical pregnancy, the antral follicle count value is found to be significantly higher ($p < 0.05$) than the group without pregnancy (Table 2).

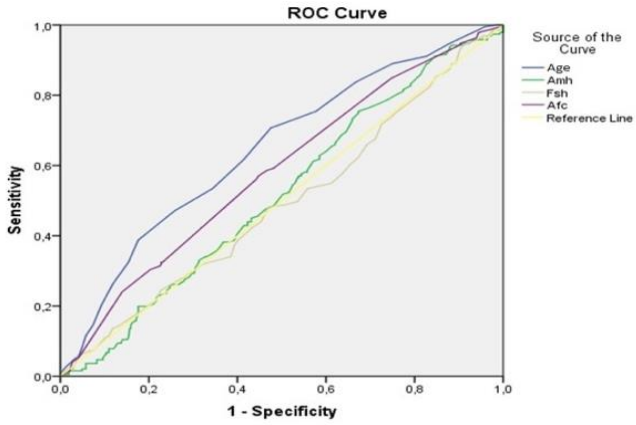
Table 2. Pregnancy prediction of variables

	Pregnancy negative, mean (min,max)	Pregnancy positive, mean (min,max)	Total, mean (min,max)	p
Age	26 (18-42)	29 (20-43)	27 (18-43)	0,000
AMH	10 (3-42)	10 (1-41)	10 (1-42)	0,513
FSH	7 (1-20)	6(1-28)	6 (0-28)	0,674
Afc	20 (8-40)	24 (8-40)	22 (8-40)	0,001

**AMH; Antimullerian hormone, FSH; Follicle-stimulating hormone, Afc; Antral Follicle Count*

As a result of AFC ROC analysis in our study for the AFC value of 20.5, the actual positivity was found to be 59 % (capture of real patients, sensitivity) was found to be 52 % (test positivity for non-patients), the area under the curve was determined as 0.58 (Figure 1).

Figure 1. Determination of variables for pregnancy



Discussion

Polycystic Ovary Syndrome (PCOS) is a common endocrinopathy in women of reproductive age and it is characterized by oligo-ovulation or anovulation, signs of hyperandrogenemia, and multiple cysts. PCOS is the most common cause of infertility for the women of reproductive age and assisted reproductive techniques are an important option with clinical pregnancy outcomes in infertile PCOS patients. In our study, in line with the literature, the difference between the clinical pregnancy outcomes of PCOS patients who received treatment and those who did not receive any treatment was found to be significant [11]. In order to apply effective protocols and appropriate treatments for these patients with infertility; firstly, it is essential to establish an appropriate diagnosis. In this study, we examined the relationship between AMH, AFC and FSH values while predicting clinical pregnancy for the PCOS patients with infertility complaints. In recent years, there have been many studies on the use of ovarian reserve markers for pregnancy and live birth prediction, and it has been stated that AMH and AFC the best indicators of ovarian reserve. Many different results have been reported in various studies that examine the relationship between AMH levels and fertilization frequencies. It has been reported that AMH shows reasonable results for predicting the quality of the embryo and oocyte as well as displaying the ovarian reserve quite successfully [18,19]. However, there are also studies that state whether the patients are suitable for IVF or not cannot be determined by AMH level and clinical pregnancy after transfer cannot be predicted by any laboratory value. There are similar studies that examine the relationship between AFC and oocyte quality, clinical pregnancy and live birth. Many studies haves been reported that measuring the number of antral follicles by ultrasonography is effective in determining the low ovarian response of patients [20]. In some studies, it has been accepted that AFC is a very strong prognostic factor for determining the response to treatment and live birth in infertility protocols. According to the study of Maseelall et al. AFC is a significant predictor of livebirth in in vitro fertilization cycles. In the same study, it was shown that AFC helps to determine appropriate treatment protocols [21]. According to another study by Muttukrishna et al., AFC has a significant relationship with the number of eggs collected and is important in predicting clinical pregnancy [22]. In our study, the role of ovarian reserve markers in the prediction of clinical pregnancy after infertility treatments of the patient group with PCOS is investigated, and the aim is to determine the threshold values that will help the patient group with a diagnosis of PCOS for clinical practice. The AMH and FSH in pregnancy prediction is not found to be significant; on the other hand, AFC is found to be statistically significant, but it is also found to be poor in diagnostic values. Studies conducted in recent years have revealed that both AMH and AFC are values that are affected by many factors, and it has been stated that a cut-off value cannot be established for clinical pregnancy prediction.

In conclusion, that this study is the first comprehensive study aimed at predicting the success of assisted reproductive techniques on AMH, AFC, and FSH levels in PCOS patients. In our study, we have found that AMH and FSH are not related to clinical pregnancy outcomes from the infertile patient group diagnosed with PCOS, and although AFC is statistically significant, it is not sufficient in diagnostic capacity. Although the positive aspect of the study is that it was conducted with more than 500 patients, the most important limitation of the present study is that it is retrospective nature. Retrospective analysis of data between 2010 and 2019 provided a larger number of data but prevented a statistically significant result as it increased the heterogeneity of the data. Therefore, there is a need for randomized controlled studies involving larger patient populations, which will create more subgroups to investigate the effect of AMH, FSH, and AFC on ART success in PCOS patients.

Disclosure

Authors have no potential conflicts of interest to disclose.

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