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Level of AMH before and after Laparoscopic Ovarian Drilling (LOD) in PCOS patients and its effect on fertility.

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Abstract

Background

Polycystic Ovarian Syndrome (PCOS) is associated with menstrual irregularities, hyper-androgenism, and polycystic ovaries. Prevalence of PCOS is around 4-18%. PCOS attribute 75% of infertility, due to lack of ovulation. PCOS patients has high level of AMH and in these patients during treatment of infertility there is possibility of developing ovarian hyperstimulation. Laparoscopic ovarian drilling (LOD) frequently performed in PCOS patients, we have decided to compare the level of AMH before and after Laparoscopic Ovarian Drilling (LOD) in these patients and its effect on fertility.

Material & Method

The present study was a cohort study consisting of 88 women with PCOS who underwent laparoscopic ovarian drilling in hitech medical college & hospital Bhubaneswar, odisha in 2021. AMH and estradiol levels of the patients were calculated before the surgery and one week after the surgery. Also, the success rate of fertility was assessed within the twelve months after the surgery, which was indicated by Intrauterine insemination (IUI) or in vitro fertilization (IVF).

Result

The relationship between mean AMH after drilling with BMI category was investigated using a one-way analysis of variance. The results showed that the mean AMH after ovarian drilling was not significantly different in the BMI categories ($P = 0.181$).

The relationship between AMH after ovarian drilling with age, BMI and previous menstrual cycle was examined using linear regression. Age and BMI variables were not significantly associated with the previous menstrual cycle (*P* > 0.05).

Conclusion

Based on the results of this study, it seems that measuring serum AMH concentration before treatment can be a useful tool in predicting LOD outcomes.

Kye words; AMH, PCOS,PCOD, LOD,IVF, anovulation, ovarian drilling.

Introduction

Polycystic Ovarian Syndrome (PCOS) is associated with menstrual irregularities, hyperandrogenism, and polycystic ovaries[1]. Prevalence of PCOS is around 4-18%. PCOS attribute 75% of infertility cases due to lack of ovulation [2]. According to a national study, the prevalence of PCOS is around 10% in India. This syndrome is also associated with features of metabolic syndrome, insulin resistance, hyperinsulinemia, and an increased risk of diabetes [4].

The pathogenesis of PCOS is complex and not fully understood. studies have revealed that insulin and androgens are the main causes of this disease [5]. Insulin predominantly affects the ovaries and the follicles. Hyper-insulinemia leads to under-development of growth of immature ovarian follicles [6]. Increased androgens and an inherent increase in the number of follicles in women with PCOS increase the production of Anti-Mullerian Hormone (AMH) [7].

People with PCOS have higher levels of testosterone, insulin, triglycerides, cholesterol , than healthy people. They also have lower levels of sex hormone-binding globulin (SHBG) and follicular growth hormone (FSH) than healthy people [7, 8]. PCOS is also associated with dyslipidemias . Other findings are prevalence of hypertension, a increased incidence of atherosclerosis and cardiovascular disease, and myocardial infarction (about 7 times higher than the healthy people) [5]. The clinical association between hyperinsulinemia and anovulation associated with hyperandrogenism is well known worldwide and among all racial groups [5]. PCOS in women, significantly reduces the quality of life [7]. These patients are at risk for various psychological changes due to metabolic disorders, especially due to changes in the level of sex hormones, especially testosterone [8–10].

The secretion of AMH gradually decreases following the growth of the follicle and is impossible in follicles larger than 8 mm [8]. Serum AMH

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concentration is associated with the number of small follicles, followed by an ovarian reserve [9]. Animal studies show that AMH has an inhibitory effect on the uptake of primordial follicles. AMH reduces the sensitivity of follicles to circulating FSH thus play an important role in folliculogenesis [10, 11]. During follicular growth, when a follicle reaches a certain size (8 mm), AMH expression decreases, as a result there is an increase in the sensitivity of the follicle to circulating FSH, thus providing an opportunity for folliclar growth until ovulation. Previous studies have shown that women with polycystic ovary syndrome have a 2 to 3 times increase in their serum AMH leading to a 2 to 3 folds increase in the number of small follicles (2–5 mm) [12, 13]. Increasing the concentration of AMH affects the pathogenesis of polycystic ovary syndrome [14]. Studies show that the aromatase enzyme is inhibited by AMH, As a result the production of follicular estradiol decreases, and this may be associated with defects in selection of dominant follicle [15].

It has been seen in studies that nutritional status and obesity have impact on AMH synthesis [13–15]. Lower levels of AMH was observed in obese women and some studies found an inverse relationship between AMH and body mass index (BMI) [17, 18], while others studies did not reported any relationship between nutritional factors, BMI, and AMH [14, 15].

PCOS patients has high level of AMH and in these patients during treatment of infertility there is possibility of developing ovarian hyperstimulation. Laparoscopic ovarian drilling (LOD) frequently performed in PCOS patients, we have decided to compare the level of AMH before and after Laparoscopic Ovarian Drilling (LOD) in these patients and its effect on fertility.

Materials and methods

The present study was a cohort study consisting of 88 women with PCOS who underwent laparoscopic ovarian drilling in hitech medical college & hospital Bhubaneswar, odisha in 2021. The sample size was calculated according to the La Marca et al. study [15] and based on the following formula, considering alpha as 0.05, d as 0.05, and P as 0.3:

$$\frac{(Z1 - \alpha/2)^2[(P(1 - P)]}{(d)^2}$$

Inclusion criteria were the PCOS patients based on the Rotterdam criteria

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(2003) [16] and are candidates for laparoscopic ovarian drilling treatment. Exclusion criteria were the patients who were not willing to participate in the study and follow-up visits.

AMH and estradiol levels of the patients were calculated before the surgery and one week after the surgery. Also, the success rate of fertility was assessed within the twelve months after the surgery, which was indicated by Intrauterine insemination (IUI) or in vitro fertilization (IVF).

Ethical considerations

informed consent was obtained from all the patients.

Table 1 Mean and standard deviation of AMH before and afterovarian drilling

Variable	Mean	Number	SD	Mean deference	*P*-value
AMH before LOD	8.8188	88	6.16	3.02	<0.001
AMH after LOD	5.7936	88		3.65	

Table 2 Menstrual cycle distribution before and after ovariandrilling

Menstrual cycle		After		Total
		Regular	Oligomenorrhe	
Before	Regular pattern	54	0	<0.001
	Oligomenorrhea	34	16	
Total		88	16	

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Statistical analysis

Descriptive results were presented as mean ± standard deviation (SD) or percentage. An independent t-test was used to compare the two means and in case of abnormal data distribution, the Mann–Whitney U test was used.

Also, McNemar's test was used to investigate the differences between binary qualitative variables. One-way analysis of variance was used to compare more than two means. Logistic regression and linear regression models were used to control the confounders. A *P*-value less than 0.05 was considered statistically significant. All data were analyzed using SPSS software version 21.

Results

The mean age of the patients was 29.10 ± 4.01 years. The mean BMI of the patients was 26.33 ± 4.14 kg/m^2. 41% of the women had normal BMI. The comparison of mean AMH before and after ovarian drilling was performed using paired t-test which showed that the mean AMH after LOD had a significant decrease ($P < 0.001$) (Table 1).

A comparison of menstrual cycle distribution before and after ovarian drilling was performed using McNemar's test which showed that there was a significant difference between menstrual cycle distribution before and after ovarian drilling ($P < 0.001$) (Table 2).

The relationship between positive or negative pregnancy with age, BMI, AMH, and the menstrual cycle was performed using logistic regression analysis, which showed that none of the variables had an effect on pregnancy ($P > 0.05$ (Table 3).

The relationship between mean AMH after drilling with BMI category was investigated using a one-way analysis of variance. The results showed that the mean AMH after ovarian drilling was not significantly different in the BMI categories ($P = 0.181$) (Table 4).

The relationship between AMH after ovarian drilling with age, BMI and previous menstrual cycle was examined using linear regression. Age and BMI variables were not significantly associated with the previous menstrual cycle ($P > 0.05$) (Table 5).

Discussion

In the present study, we compared the level of AMH before and after laparoscopic ovarian drilling in patients with PCOS and its effect on fertility.

In a prospective cohort study performed by Elmashad et al., a significant decrease in serum AMH levels of the patients with PCOS was observed in the post-treatment phase and the final result indicates the role of AMH before laparoscopic ovarian drilling in predicting out- comes [17]. The results of this study were consistent with our study.

In a prospective cohort study performed by Farzadi et al. in Iran on 30 women with PCOS who underwent laparoscopic ovarian drilling, it was reported that there was a significant decrease in the serum AMH level in the post-treatment phase. The mean AMH before treatment was 8.4 ng/ml, one week, three months, and six months later were 7.5 ng/ml, 7 ng/ml, and 7.7 ng/ml respectively, indicating that this treatment did not cause a change in ovarian reserve [18].

A review study by Amer et al. in the UK on AMH levels in women with PCOS under laparoscopic ovarian drill- ing found a significant reduction in serum AMH levels by 2.13 ng/ml in these patients.

Table 3 Logistic regression analysis of the relationship between positive or negative pregnancy dimensions with age, BMI, AMH dimension, and menstrual cycle

Variables	B	Std. Error (SD)	Odds Ratio (OR)	95% Confidence interval		*P*-Value
				Lower	Upper	
Age	-0.064	0.079	0.938	0.804	1.095	0.418
BMI	0.048	0.071	1.050	0.913	1.206	0.495
AMH after	-0.058	0.087	0.944	0.796	1.120	0.507
Menes after	1.916	1.178	6.794	0.676	68.311	0.104

Table 4 Mean AMH after ovarian drilling across BMI category

BMI (kg/m^2)	Number	Mean	SD	95% Confidence for Mean Interval	*P*-value

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				Lower Bound	Upper Bound	
18.5–25	32	5.13	3.37	3.9156	6.3469	0.181
25–30	31	6.73	4.00	5.2651	8.2058	
30–35	15	5.26	3.25	3.4567	7.0633	
Total	78	5.79	3.65	4.9695	6.6177	

Table 5 Linear regression results to evaluate the relationship between AMH after ovarian drilling with age, BMI, and previous menstrual cycle

Variables	Unstandardized Coefficients		95.0% Confidence Interval		*P*-value
	B	Std. Error	Lower Bound	Upper Bound	
Constant	3.989	3.271	-2.529	10.506	0.227
Age (year)	-0.100	0.091	-0.283	0.082	0.276
BMI (kg/m^2)	-0.029	0.093	-0.214	0.156	0.754
Previous menstrual cycle	3.826	0.761	2.310	5.343	< 0.001

In the post-treatment phase, it is observed that it is not clear whether this reduction is only within normal limits, such as in women without PCOS, or reduces ovarian reserve [19]. The results of this study were consistent with the present study.

A study done by Abu Hashim et al. in Egypt on serum AMH levels in women with PCOS under laparoscopic ovarian drilling in unilateral and bilateral cases reported a decrease in serum AMH levels in unilateral and bilateral laparoscopic cases [20]. This study also had consistent results with the present study.

An analytical study was conducted by Giampaolino et al. in Italy on 123 women with PCOS under laparoscopic ovarian drilling and 123 women with PCOS under Trans-

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vaginal hydro-laparoscopy (THL). Both methods showed that the rate of reduction was similar in the two methods [21].

In a prospective cohort study conducted by Par- amu et al. in India on 30 women with PCOS under laparoscopic ovarian drilling, there was a significant reduction of up to 33% in the serum AMH level in the post-treatment phase [22]. The results of Paramu et al. and Gaafar et al.'s studies were consistent with the present study [22, 23].

Previous studies have concluded that a decrease in AMH after LOD should be considered a normalization process rather than a pathological decrease in ovarian reserve. Mild ovarian injury inefficiencies in performing LOD with four to five holes in the ovary are more effective than performing only two or fewer holes [22, 24, 25].It is suggested that the increase in AMH levels in patients with PCOS is due to an increase in the number of primary antral follicles [26]. However, other reports have shown that the increase in AMH concentration is mainly due to the increase in AMH production by each follicle and is not just the result of an increase in the number of follicles [27]. AMH may be a marker of ovarian aging because it is associated with the number of primary antral follicles which indicates the size of the follicle rest chamber, so if AMH levels decrease, the ovarian reserve may be compromised [28].

The question is whether laparoscopy affects ovarian tissue and reduces ovarian reserve. Weerakiet et al. examined changes in serum AMH levels before and after LOD [29]. They found that the mean changes in serum levels of AMH in 21 patients with PCOS were three days after LOD, which was not statistically significant. In our study, mean levels of AMH did not change significantly before laparoscopy, 1 week, 3 months, and 6 months after laparoscopy.

AMH is considered an important marker of ovarian reserve [30]. Serum AMH is 2–4 times higher in women with PCOS than in healthy women. This is because PCOM ovaries show the number of small antral follicles producing AMH [31] and increase production in granulosa cells [32]. An acceptable explanation for the decrease in serum AMH after LOD could be the effect of heat damage, which reduces its production from the granulosa cells of the primary, pre-abdominal, and small antral follicles [20].

Conclusion

Based on the results of this study, it seems that measuring serum AMH concentration

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before treatment can be a useful tool in predicting LOD outcomes. This also can help in choosing a suitable patient for the treatment. Further studies are needed to determine more accurately whether AMH is the cause or outcome of ovulation after surgery.

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