

## Effect of Laparoscopic Ovarian Drilling on Outcomes of In-Vitro Fertilization in Clomiphene-Resistant Women with Polycystic Ovary Syndrome

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### ABSTRACT

**Background:** The polycystic ovarian syndrome is associated with anovulation and infertility. Recently the laparoscopic ovarian drilling (LOD) has been used as a surgical treatment for ovulation in women with polycystic ovarian syndrome (PCOS), although its mechanism and outcomes are still unclear. The purpose of this study is to evaluate the LOD effect before *in vitro* fertilization (IVF) / intracytoplasmic sperm injection (ICSI) in clomiphene-resistant women with PCOS.

**Objective:** To evaluate the effect of LOD on the outcome of IVF/ICSI cycle in Clomiphene-Resistant women with PCOS as regards pregnancy rate.

**Patients and Methods:** The current study, included a total of 88 women with history of clomiphene-resistant PCOS, who had been distributed into two groups: Group A (N=44): clomiphene-resistant PCOS women who has history of LOD at least 6 months to 3 years before IVF/ICSI. Group B (N=44): clomiphene-resistant PCOS women without history of drilling. All women were from 20 to 35 years old with at least one year infertility and BMI <30, and none of them has history of previous IVF/ICSI or history of any chronic disease such as thyroid disorder, DM and sever endometriosis.

**Results:** A significant decrease was observed in the number of AFC among patients with history of LOD than among patients in no LOD group. In our present study, regarding hormonal profile (FSH, LH, E2, PRL & TSH), despite that the serum concentration of LH and FSH were lower among patients in LOD group than in no LOD group but this difference did not reach significance. The chemical and clinical pregnancy rate as the primary outcome were significantly higher among women with history of than among women with no history of LOD. As regard the incidence of OHSS, known as a potential life-threatening disorder there was no statistical difference between both study groups.

**Conclusion:** LOD is method of treatment of PCO females with failure medical treatments (clomiphene-resistant). Clinical pregnancy rate was significantly higher in women with history of LOD than among women with no history of LOD (34.1% and 15.9% respectively).

**Key Words:** Intracytoplasmic sperm injection, laparoscopic ovarian drilling, polycystic ovary.

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### INTRODUCTION

Polycystic ovary (PCO) is considered as one of the most common endocrine disorders. It occurs in 6-21% of women. It is the primary cause of an-ovulatory subfertility, accounting for at least 75% of cases with an-ovulatory subfertility<sup>[1]</sup>.

Lifestyle modifications and clomiphene citrate (CC), a selective estrogen receptor modulator, still remain the first line of treatment for PCOS patients<sup>[2]</sup>. However, between 15 - 40 % of PCO patients show persistent anovulation following treatment with clomiphene citrate and they are considered to have clomiphene citrate-resistant PCOS<sup>[3]</sup>.

Eventually, LOD has become the preferred surgical alternative for ovulation induction in clomiphene citrate-resistant PCOS patients<sup>[4]</sup>.

LOD has been proposed as an alternative to treatment of clomiphene-resistant patients with PCOS due to its quick and easy approach<sup>[5]</sup>.

A study has reported that the impact of LOD prior to ART is beneficial in decreasing the OHSS risk and improving the pregnancy rate in women with a history of cancellation of IVF cycle due to risk of OHSS<sup>[6]</sup>.

Another study has showed that ovarian trauma disrupts local androgen synthesis that leads to a reduction in intra-ovarian androgen concentration that is followed by negative effects of androgen on follicular maturation. Subsequently it results in decreased peripheral conversion of androgen to estrogen that cause positive feedback on LH secretion<sup>[7]</sup>.

The effect of LOD on ART outcomes in clomiphene-resistant PCOS patients is still unknown; therefore, this study aimed to evaluate IVF/ICSI outcomes in clomiphene-resistant women with PCOS who were treated with LOD.

## AIM OF THE WORK

The aim of the study is to evaluate the effect of LOD on the outcome of IVF/ICSI cycle in Clomiphene-Resistant women with PCOS as regards pregnancy rate.

## PATIENTS AND METHODS

### Type of study

Prospective cohort study.

### Study setting

This study was conducted at Ain Shams Maternity Hospital at the Assisted Reproductive Technology unit, during the period from August 2018 to September 2019.

### Study population

A total of 88 women with history of clomiphene-resistant PCOS who had an-ovulatory infertility and were nominated for IVF/ICSI, had been enrolled in this study distributed into two groups: Group A (N=44): clomiphene-resistant PCOS women who has history of LOD at least 6 months to 3 years before IVF/ICSI. Group B (N=44): clomiphene-resistant PCOS women without history of drilling.

### Inclusion criteria

Age between 20 and 35. Patients with established PCOS diagnosed by having at least 2 signs of the following Rotterdam criteria: Anovulation or oligomenorrhea. Clinical (hirsutism, alopecia and android changes in the body) or biochemical (elevated free testosterone, free androgen index or bioavailable testosterone) signs of hyperandrogenism. The typical ultrasound pattern of polycystic ovaries (follicle number per ovary =20 and/or an ovarian volume =10 ml on either ovary, ensuring no corpora lutea, cysts or dominant follicles are present. History of at least one year infertility. No response to clomiphene citrate for at least three cycles (failure to ovulate after receiving 150 mg of CC daily for 5 days per cycle, for at least 3 cycles).

### Exclusion criteria

History of previous IVF/ICSI. Chronic disease such as thyroid disorder and DM. Infertility due to sever male factor (azoospermia). Sever endometriosis. Infertility due

to uterine factor such as multiple fibroids. Body mass index > 30.

### Study outcomes

**Primary outcome:** clinical pregnancy rate. Secondary outcomes: Induction of ovulation (dose and duration). Risk of OHSS. Number of oocytes collected. Quality of embryos transferred.

### Statistical analysis

The required sample size has been calculated using the G\*Power Software (Universität Düsseldorf, Germany).

The primary outcome measure is the clinical pregnancy rate. Currently, there is no adequate information regarding the effect of LOD on the occurrence of clinical pregnancy in clomiphene-resistant PCO patients. Therefore, the current exploratory study would target an effect size that could be regarded as clinically relevant.

So, it is estimated that a sample size of 44 patients in either study group (total, 88 patients) would achieve a power of 80% (type II error = 0.2) to detect a statistically significant difference between the 2 groups as regards the clinical pregnancy rate for a medium effect size corresponding to a w of 0.3 using a two-sided chi-squared test with 1 degree of freedom and the targeted test confidence set at a level of 95% (type I error = 0.05). The effect size (w) is calculated as follows:

$w = \sqrt{\frac{\chi^2}{N}}$ , where  $\chi^2$  is the chi-squared statistic and N is the total sample size<sup>[8]</sup>.

The targeted effect size of w = 0.3 has been selected as it could be regarded as a clinically relevant difference to seek in this exploratory study.

Ethical consideration A written informed consent was obtained from all participants before screening and enrollment. Participants participated voluntarily in the research and their confidentiality had been respected. Benefits from participation in the research were explained to all participants after approval of research ethical committee.

### Study procedures

All participants were subjected to the following: Detailed medical history including: Personal history. Menstrual history. Past and obstetric history Physical examination: Complete examination was recorded including BMI in kg/m<sup>2</sup>. Laboratory investigations: Routine investigations including; Hormonal profile, LH/FSH ratio.

Induction of ovulation: On day 3 of spontaneous cycles, all patients had basal hormonal profile (FSH, LH, E2, TSH and prolactin). Transvaginal (TV) ultrasound (U/S) on day 3 of non-stimulated cycles was done by TV probe of 5-9 MHZ. Any patient found to have uterine abnormalities was excluded. Ovarian stimulation was held according to a long GnRH agonist protocol starting from midluteal phase by daily SC injection of triptoreline acetate (Decapeptyl 0.05 mg). Then on day 3 of next cycle ovarian hyper stimulation was started by daily injection of HMG (Menogon 75 IU/amp. or Merional 75 IU/amp.). The starting dose of gonadotropins was prescribed according to the age and body weight of the subjects, then the dose was adjusted according to the ovarian response that will be assessed by TV folliculometry which was started on cycle day six. According to the ovarian response, every other day TV U/S had been performed and at the moment when the leading follicle reaches 16mm, daily TV U/S had been performed till the largest follicle reach a diameter of >18mm. HCG (Chorimom 10,000 IU/amp.) was administered for triggering ovulation.

### ***Ovum pick up***

34-36 hours after HCG injection, the transducer was connected to the U/S system. The direction of the guide beam was checked. The puncturing needle was connected to an aspiration apparatus attached by a fixation ring to the front and rear ends of the TV transducer, thereby defining the direction of puncture corresponding to the guide beam on the U/S image. The aspiration was checked using test tubes. The uterus, both ovaries and iliac vessels were identified by the visualization in both planes. The distance between the upper pole of the vagina and the ovary was closely evaluated (care had been taken to avoid intestinal or vascular interposition). Depth localization of the closest accessible follicle (distance from the upper vaginal pole to the center of the follicle) was done. Needle was pushed forcefully to the center of the follicle (Aspiration pressure 90-100mmHg).

### ***IVF- ICSI***

ICSI was performed on metaphase II oocytes using the direct penetration technique, fertilization results were assessed 16 to 19 hours after ICSI. Fertilization was considered normal by the presence of two pronuclei and/ or 2nd polar body. Oocyte degeneration was identified by collapse of cytoplasmic contents and separation from the zona. Failed fertilization was defined by the absence of the pronuclei.

### ***Embryo transfer***

Embryo transfer was done on 3rd day or 5<sup>th</sup> day post insemination using cook catheter under U/S guide at

a distance about 1-1.5 cm from the fundus by the same gynecologist. № of max. embryos transferred 3 embryos on day 3 & 2 embryos on day 5.

### ***Finally***

A serum  $\beta$ hCG was done 12 days after embryo transfer and repeated after 48h. followed by U/S 6 weeks after embryo transfer.

### ***Statistical methods***

Data were analyzed using IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY). Numerical variables were presented as mean and SD and inter-group differences were compared using the unpaired t-test. Categorical variables were presented as ratio or as number and percentage and differences were compared using the Pearson chi-squared test or Fisher's exact test if appropriate. Ordinal data were compared using the chi-squared test for trend. Multivariable binary logistic regression analysis was used to examine the effect of LOD on occurrence of pregnancy as adjusted for other confounding factors. Two-sided *p-values* <0.05 were considered statistically significant.

## **RESULTS**

Table 1 show no significant difference between the studied groups regarding demographic characteristics.

Table 2 shows no significant difference between he studied groups regarding the hormonal profile.

Table 3 shows significant decrease in the AFC in women with history of LOD.

Table 4 shows no significant difference between studied groups regarding the duration of stimulation and the number of HMG ampoules.

Table 5 shows no significant difference between the two groups regarding the number of oocytes collected and number of produced embryos.

Table 6 shows no significant difference between both study groups regarding the number of transferred embryos, embryos transfer day and best grade of transferred embryos.

Table 7 shows significant increase in chemical and clinical pregnancy rate in women with history of LOD.

Table 8: shows no significant difference in the incidence of OHSS in both study groups.

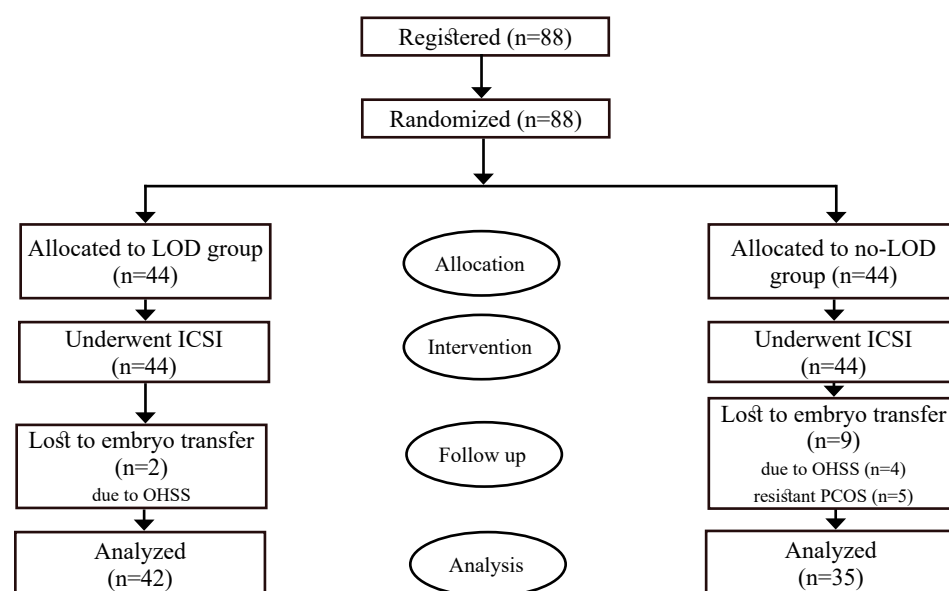


Fig. 1: CONSORT, patients flow chart

Table 1: Demographic characteristics among the studied groups

Items	Measure	No LOD (N=44)	LOD (N=44)	P
Age (years)	Mean±SD	28.9±3.6	28.1±4.2	0.371*
	Range	35.0–22.0	35.0–20.0	
BMI (kg/m <sup>2</sup> )	Mean±SD	25.2±2.9	24.5±2.8	0.209*
	Range	29.6–19.3	29.4–20.4	
Infertility duration (years)	Mean±SD	4.8±2.6	4.2±2.4	0.223*
	Range	12.0–1.0	11.0–1.0	
Type (% ,n)	Primary	(77.3%) 34	(81.8%) 36	0.597§
	Secondary	(22.7%) 10	(18.2%) 8	

Data are mean ± SD

\*Unpaired t-test unless otherwise indicated.

§Pearson chi-squares test.

Table 2: Hormonal profile in both study groups.

Variable	No LOD (n=44)		LOD (n=44)		Mean Difference	CI 95%		P-value*
	Mean	SD	Mean	SD		Lower	Upper	
FSH (mIU/ml)	6.48	2.82	6.31	1.91	0.167	-0.854	1.188	0.746
LH (mIU/ml)	7.48	5.97	6.16	2.78	1.318	-3.293	0.656	0.188
E2 (pg/ml)	49.5	23.9	62.5	82.2	-13.041	-38.972	12.890	0.317
Prolactin (ng/ml)	14.6	6.3	15.9	7.5	-1.305	-4.235	1.626	0.379
TSH (mIU/l)	2.28	1.22	1.98	0.94	0.295	-0.168	0.758	0.208

Data are mean and standard deviation (SD).

95% CI = 95% confidence interval.

\*Unpaired t-test

Table 3: AFC in both study groups.

Variable	No LOD (n=44)		LOD (n=44)		Mean Difference	CI 95%		P-value
	Mean	SD	Mean	SD		Lower	Upper	
AFC	19	6	15	8	3.886	-6.883	-0.890	0.012

Data are mean and standard deviation (SD).

95% CI = 95% confidence interval.

\*Unpaired t-test

**Table 4:** Duration of stimulation and number of HMG ampoules in both study groups.

Variable	No LOD (n=44)		LOD (n=44)		Mean Difference	CI 95%		*P-value
	Mean	SD	Mean	SD		Lower	Upper	
(Duration of stimulation (days	12	3	13	3	-0.568	-1.861	0.724	0.385
Number of HMG ampoules	43	18	36	16	6.818	-0.326	13.962	0.061

Data are mean and standard deviation (SD).

95% CI = 95% confidence interval.

\*Unpaired t-test

**Table 5:** Number of oocytes and produced embryos in both study groups.

Variable	No LOD (n=44)		LOD (n=44)		Mean Difference	CI 95%		*P-value
	Mean	SD	Mean	SD		Lower	Upper	
Number of oocytes	6	4	7	5	-1.750	-3.828	0.328	0.098
Number of produced embryos	4	3	5	4	-1.136	-2.714	0.441	0.156

Data are mean and standard deviation (SD).

95% CI = 95% confidence interval.

\*Unpaired t-test

**Table 6:** Number and grade of transferred embryos in both study groups.

Variable		No LOD (n=44)		LOD (n=44)		$\chi^2(df,1)$	*P-value
		n	%	n	%		
Number of transferred embryos	No embryo transferred	9	20.5%	2	4.5%	1.486	0.223
	Embryo 1	8	18.2%	9	20.5%		
	Embryos 2	9	20.5%	16	36.4%		
	Embryos 3	18	40.9%	17	38.6%		
Embryo transfer day	D3	25	74.3%	28	66.7%	1.619	0.203
	D5	10	25.7%	14	33.3%		
	Grade A	29	82.9%	38	88.4%		
Best grade of transferred embryos	Grade B	4	11.4%	2	4.7%	0.239	0.625
	Grade C	0	0.0%	2	4.7%		
	Morula	2	5.7%	1	2.3%		

Data are number (n) and percentage (%).

 $X^2$  = chi-squared statistic, df = 1 degree of freedom.

\*Chi-squared test for trend.

**Table 7:** Pregnancy rate in both study groups.

Variable		No LOD (n=44)		LOD (n=44)		$\chi^2(df,1)$	*P-value
		n	%	n	%		
Chemical pregnancy	Negative	36	81.8%	27	61.4%	4.526	0.033
	Positive	8	18.2%	17	38.6%		
Clinical pregnancy	Negative	37	84.1%	29	65.9%	3.879	0.049
	Positive	7	15.9%	15	34.1%		

Data are number (n) and percentage (%).

 $X^2$  = chi-squared statistic, df = 1 degree of freedom.

\*Pearson chi-squared test.

**Table 8:** Incidence of OHSS in both study groups.

Variable		No LOD (n=44)		LOD (n=44)		*P-value
		n	%	n	%	
OHSS	Negative	40	90.9%	43	97.7%	0.360
	Positive	4	9.1%	1	2.3%	

Data are number (n) and percentage (%).

\*Fisher's exact test.

## DISCUSSION

Polycystic ovary syndrome (PCOS) is a heterogeneous condition characterized by hyperandrogenism, ovarian dysfunction and polycystic ovarian morphology (PCOM), PCOS is more than just a reproductive disorder, and is currently considered a syndrome with metabolic consequences that could affect women's health during different stages of reproductive and post-reproductive life<sup>[9,10]</sup>.

Recently laparoscopic ovarian drilling (LOD) has been used widely by gynecologists as an alternative surgical method for ovulation induction using gonadotropins for PCOS patients unresponsive to clomiphene<sup>[11]</sup>.

LOD has been proposed as an alternative to treatment of clomiphene-resistant patients with PCOS due to its quick and easy approach<sup>[5]</sup>.

A study has reported that the impact of LOD prior to ART is beneficial in decreasing the OHSS risk and improving the pregnancy rate in women with a history of cancellation of IVF cycle due to risk of OHSS<sup>[6]</sup>.

The effect of LOD on ART outcomes in clomiphene-resistant PCOS patients is still unknown; therefore, this study aimed to evaluate IVF/ICSI outcomes in clomiphene-resistant women with PCOS who were treated with LOD.

In this study, we evaluated the IVF/ICSI outcome in a total of 88 women with history of clomiphene-resistant PCOS, who had been distributed into two groups: Group A (N=44): clomiphene-resistant PCOS women who has history of LOD at least 6 months to 3 years before IVF/ICSI. Group B (N=44): clomiphene-resistant PCOS women without history of drilling.

All women were from 20 to 35 years old with at least one year infertility and BMI <30, and none of them has history of previous IVF/ICSI or history of any chronic disease such as thyroid disorder, DM and sever endometriosis.

On day 3 of spontaneous cycles, all patients had basal hormonal profile (FSH, LH, E2, TSH and prolactin) and transvaginal (TV) ultrasound (U/S).

Ovarian stimulation was held according to a long GnRH agonist protocol and ICSI and embryo transfer was performed.

Finally, A serum  $\beta$ hCG was done 12 days after embryo transfer and repeated after 48h. followed by U/S 6 weeks after embryo transfer.

In this current study, the clinical characteristics were apparently similar among both study group with no

significant difference, the mean age among LOD group was  $28.1 \pm 4.2$  and  $28.9 \pm 3.6$  among no LOD group, the mean BMI was  $24.5 \pm 2.8$  and  $25.2 \pm 2.9$  in LOD AND no LOD groups respectively. As regards the mean duration of infertility in LOD group was  $4.2 \pm 2.4$  and  $4.8 \pm 2.6$  in no LOD group. The 1ry infertility ratio was 81.1% in LOD and 77.3% in no LOD group while 2ry infertility ratio was 18.2% and 22.7% in LOD and no LOD group respectively. (Table 1)

A significant decrease was observed in the number of AFC among patients with history of LOD ( $19 \pm 6$ ) than among patients in no LOD group ( $15 \pm 8$ ) with P-value=0.012 (Table 3).

This finding found to be in accordance with the results of previous prospective controlled study evaluated the effect of laparoscopic ovarian drilling (LOD) on plasma levels of anti-Müllerian hormone (AMH) and ovarian stromal blood flow changes, by using three-dimensional power Doppler ultrasonography, in PCOS<sup>[12]</sup>.

According to Elmashad's results there was significant reduction in the mean AFC after LOD ( $15.0 \pm 2.2$ ) than before LOD ( $29.0 \pm 2.4$ ). This could be explained by possible damage to the ovarian blood vessels and ovarian parenchyma after bipolar electrocoagulation during laparoscopy.

In our present study, regarding hormonal profile (FSH, LH, E2, PRL & TSH), despite that the serum concentration of LH and FSH were lower among patients in LOD group ( $6.16 \pm 2.78$  and  $6.31 \pm 1.91$  respectively) than in no LOD group ( $7.48 \pm 5.97$  and  $6.48 \pm 2.82$  respectively) but this difference did not reach significance. (Table 2)

In agreement with this results, Elmashad (12) reported the same results as they found that the level of LH and FSH were lower in LOD group but with no statistical significance.

In contrast to our results, Amer *et al.*<sup>[11]</sup> study that investigated the long-term follow-up of patients with PCOS after LOD: endocrine and ultrasonographic outcome, included 116 women with polycystic ovary syndrome (PCOS) who had laparoscopic ovarian drilling (LOD) for anovulatory infertility and 34 anovulatory PCOS women who had not undergone LOD, resulted in significant decrease in the LH:FSH ratio, mean serum concentrations of LH and testosterone and free androgen index after LOD and remained low during the medium- and long-term follow-up periods.

In this current study, there was no significant difference observed in the duration of induction between both study group. And as regard the dose of induction it was higher among women with no history of LOD than women with

history of LOD (mean 43, SD 18 and mean 36, SD 16 respectively) but this difference was of no significance statistically (Table 4).

In agreement with our study, Breborowicz *et al.*<sup>[13]</sup> in a prospective study evaluated the effect of transvaginal LOD on women with sever PCOS prior to IVF, and the results showed that there were no significant differences in peak estradiol, gonadotropin dose, or days of stimulation.

Also in accordance with our results, Tozer *et al.*<sup>[14]</sup> conducted a retrospective comparative study aimed to evaluate the effect of LOD on the outcome of IVF- embryo transfer in women with PCOS. 31 women were recruited and divided into 2 arms. Group A (included 15 women previously undergone LOD) and group B (included 16 women had not undergone LOD). And they found that there were no differences observed between the two groups in the amount of gonadotrophin required for ovarian stimulation.

But in contrast to our study, Farhi *et al.*<sup>[15]</sup> in a retrospective study evaluated the effect of laparoscopic ovarian electrocautery on ovarian response and outcome of treatment gonadotropines in CC resistant patients with PCOS, their results concluded that there were significant reduction in the number of ampules, daily effective dose and duration of the induction phase after laparoscopic ovarian electrocautery.

Neither the mean number of oocytes retrieved nor the mean number of produced embryos were statistically significantly different between both groups, although there appeared to be more oocytes retrieved and more embryos produced patients in LOD group, as shown in Table 5.

Tozer *et al.*<sup>[14]</sup> in their study reported that, while there appeared to be more oocytes retrieved in group B ( $14.3 \pm 4.9$  versus  $11.8 \pm 7.3$ ), this was not statistically significantly different, which came in agreement with our study.

The same study resulted in a statistically significant greater number of embryos available for transfer in group B than in group A ( $7.1 \pm 3.8$  versus  $4.6 \pm 2.7$ ;  $P < 0.01$ ) which contradict our results<sup>[14]</sup>.

Also in disagreement with our study, a retrospective study by Cai *et al.*<sup>[16]</sup>, performed to determine if history of LOD was associated with changes in cumulative ongoing pregnancy rates among patients with PCOS undergoing IVF. The study included 110 patients in the LOD group, 127 patients in the no LOD group and 990 patients in the age matched group. They resulted in significantly lower number of retrieved oocytes and available embryos were observed in patients who had a history of LOD in comparison with patients in the no LOD and age matched groups ( $P$ -value  $\leq 0.001$  for all comparisons).

When considering the number of transferred embryos, the percentage of patients that had one, two or three embryos transferred did not differ between the two groups, with most patients underwent transfer of three embryos (40.9% and 38.6% in no LOD and LOD patients respectively) (Table 6).

The percentage of patients who did not transfer any embryos either due to OHSS or resistant PCOS no oocytes retrieved, was apparently higher in no LOD group (9 patients =20.5%) than LOD group (2 patients =4.5%) but this difference was of no statistical significance (Table 6).

Among the 35 patients who underwent embryo transfer in the no LOD group, 25 patients (74.3%) had a day 3 transfer and 10 patients (25.7%) had a day 5 transfer and among the 42 patients who underwent embryo transfer in LOD group, 28 patients (66.7%) had a day 3 transfer and 14 patients (33.3%) has a day 5 transfer, but these differences were not statistically significant (Table 6).

As regard the quality of embryos: embryos grade A was higher in LOD (88.4%) than in no LOD group (82.9%), embryos grade B was higher in no LOD (11.4%) than in LOD group (4.7%), there were no embryos grade C transferred in the no LOD group compared to the LOD group (4.7%) and embryos grade morula was higher in no LOD (5.7%) than in LOD group (2.3%), but this difference between both study groups is of no statistical significance as shown in (Table 6).

Cai, *et al.*<sup>[16]</sup>, their results came in agreement with our current study regarding the number and quality of embryos transferred (no significant difference in percentages of patients in both study groups).

But the same study results disagreed with our results as regard the percentage of canceled embryo transfer as they found that the rate of cancelled embryo transfer was significantly higher among patients in no LOD group in comparison with the LOD group ( $P$ -value= 0.016) (16).

Based on our results, the chemical and clinical pregnancy rate as the primary outcome were significantly higher among women with history of LOD (38.6% and 34.1% respectively with  $P$ -value=0.033) than among women with no history of LOD (18.2% and 15.9% respectively with  $P$ -value =0.049) (Table 7).

This could be explained by, lower concentration of LH following the ovarian drilling which is previously reported to be the main mechanism by which the reproductive outcome is improved, with elevated concentration of serum LH being associated with reduction in oocytes quality, fertilization rate and embryo quality<sup>[17,18]</sup>.

In this study, it was observed that the mean concentration of LH was lower after laparoscopic ovarian drilling, the number of oocytes and embryos available for transfer were higher after the surgery, and best grade of embryos transferred was higher in the LOD group. Although these differences did not reach statistical significance but this might explain the significant increase in pregnancy rate among the patients in LOD group.

In agreement with our study, Breborowicz *et al.*<sup>[13]</sup>, they found that TVOD resulted in significant improvement in outcome parameters and it quadrupled the implantation (implantation rate in pre-TVOD group was 6.1% while in post-TVOD group was 35.9% with *P* value of 0.004), clinical pregnancy (clinical pregnancy rate in pre-TVOD group was 11.8% while in post-TVOD group was 60% with *P* value of 0.01) and ongoing pregnancy rate (ongoing pregnancy rate in pre-TVOD was 5.9% while in post-TVOD was 40% with *P* value 0.05).

Also, in accordance with our study, Colacurci *et al.*<sup>[19]</sup>, they designed a prospective study to compare IVF stimulation parameters and pregnancy rate for two groups of women with polycystic ovarian syndrome. In the first group, we included 23 patients previously treated by laparoscopic ovarian electrodiathermy (group A), in the second group we included 36 women who did not undergo surgical treatment (group B). They found a significantly higher ongoing pregnancy rate (28.6%) in group A vs. (7.3%) in group B with *P*-value < 0.05.

But in disagreement with our study, Tozer *et al.*<sup>[14]</sup> in their study found that there is no significant difference between the two groups of their study as regard pregnancy rate per cycle, or per embryo transfer.

As regard the incidence of OHSS, known as a potential life-threatening disorder, 4 patients among 44 patients with no history of LOD (9.1%) were diagnosed with OHSS compared to 1 patient among the patients with history of LOD (2.3%), but this difference was not statistically significant (Table 8).

In disagreement with our study, Eftekhari *et al.*<sup>[7]</sup> study which was retrospective study investigating the effect of LOD on the outcomes of IVF in clomiphene-resistant women with PCOS. A total of 300 women were enrolled in the study and the result showed that ovarian cauterization before IVF/ICSI in patients with PCOS reduced the risk of OHSS (*P*=0.025). Despite the same pregnancy rate in both groups (*P*=0.604), more obtained oocytes and embryos were seen on women without ovarian drilling than women with LOD (*P*<0.001 and *P*=0.033, respectively).

## CONCLUSION

LOD is method of treatment of PCO females with failure medical treatments (clomiphene-resistant). Clinical

pregnancy rate was significantly higher in women with history of LOD than among women with no history of LOD (34.1% and 15.9% respectively).

## CONFLICT OF INTERESTS

There are no conflicts of interest.

## REFERENCES

1. Joham AE, Teede HJ, Ranasinha S, Zoungas S and Boyle J. (2015): Prevalence of infertility and use of fertility treatment in women with polycystic ovary syndrome: data from a large community-based cohort study. *J Womens Health*, 24(4): 299-307.
2. Mitra S, Nayak PK and Agrawal S. (2015): Laparoscopic ovarian drilling: an alternative but not the ultimate in the management of polycystic ovary syndrome. *J Nat Sci Biol Med*, 6(1):40-48.
3. Abu Hashim H, Foda O and Ghayaty E. (2015): Combined metformin- clomiphene in clomiphene-resistant polycystic ovary syndrome: a systematic review and meta-analysis of randomized controlled trials. *Acta Obstet Gynecol Scand*, 94: 921-930.
4. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, Lizneva D and Natterson-Horowitz B. (2016): Polycystic ovary syndrome. *Nat Rev Dis Primers*, 2016; 2:16057.
5. Flyckt RL and Goldberg JM (2011): Laparoscopic ovarian drilling for clomiphene-resistant polycystic ovary syndrome. *Semin Reprod Med*, 29(2): 138-146.
6. Lebbi I, Ben Temime R, Fadhlaoui A and Feki A. (2015): Ovarian Drilling in PCOS: Is it Really Useful? *Front Surg*, 2: 30.
7. Eftekhari M, Dehghani Firoozabadi R, Khani P, Ziaei Bideh E and Forghani H. (2016): Effect of laparoscopic ovarian drilling on outcome of IVF in clomiphene-resistant PCOS women. *Int J Fertil Steril*, 10(1): 42-47.
8. Chow SC, Shao J and Wang H. (2003): *Sample Size Calculations in Clinical Research*. First ed. New York: Marcel Dekker Inc.
9. Dunaif A and Fauser BC. (2013): Renaming PCOS-a two-state solution. *J Clin Endocrinol Metab*, 98(11): 4325-4328.
10. Orio F and Palomba S. (2014): Reproductive endocrinology: new guidelines for the diagnosis and treatment of PCOS. *Nat Rev Endocrinol*, 10:130-132.



11. Amer SA, Banu Z, Li TC, Cooke ID (2002): Long term follow up of patients with polycystic ovary syndrome after laparoscopic ovarian drilling: endocrine and ultrasonographic outcomes. *Human Reprod*, 17(11):2851-2857.
12. Elmashad A. (2011): Impact of laparoscopic ovarian drilling on anti-Mullerian hormone levels and ovarian stromal blood flow using three-dimensional power Doppler in women with anovulatory polycystic ovary syndrome. *Fertil Steril*, 95(7): 2342-2346.
13. Breborowicz AK, Keltz MD, Chau P, Stein D, Lederman M and Gonzales E (2012): Transvaginal ovarian drilling (TVOD) for severe polycystic ovary syndrome (PCOS) prior to *in vitro* fertilization (IVF) improves outcomes. *Fertil Steril*, 98(3):S212-S212.
14. Tozer AJ, Al-Shawaf T, Zosmer A, Hussain S, Wilson C, Lower AM and Grudzinski JG. (2001): Does laparoscopic ovarian diathermy affect the outcome of IVF-embryo transfer in women with polycystic ovarian syndrome? A retrospective comparative study. *Hum Reprod*, 16(1):91-95.
15. Farhi J, Goule S and Jacobs H. (1995): Effect of laparoscopic ovarian electrocautery on ovarian response and outcome of treatment with gonadotrophins in clomiphene citrate resistant patients with PCOS. *Fertil Steril*, 64: 930-935.
16. Cai J, Liu L, Sun L, Sha A, Jiang X and Ren J. (2016): Effect of previous ovarian drilling on cumulative ongoing pregnancy rates among patients with polycystic ovarian syndrome undergoing *in vitro* fertilization. *Int J Gynecol Obst*, 134: 272-277.
17. Stanger J. and Yovich J. (1985): Reduced *in-vitro* fertilisation of human oocytes from patients with raised basal luteinising hormone levels during the follicular phase. *Br J Obstet Gynaecol*, 92: 385-393.
18. Urman B, Fluker M, Yuen BH, Bettina G, Christo G, Young S. (1992): The outcome of *in vitro* fertilisation and embryo transfer in women with polycystic ovarian syndrome failing to conceive after ovulation induction with exogenous gonadotrophins. *Fertil Steril*, 57: 1269-1273.
19. Colacurci N, Zullo F, De Franciscis P, Mollo A and De Placido G. (1997): *In vitro* fertilization following laparoscopic ovarian diathermy in patients with polycystic ovarian syndrome. *Acta Obstet Gynecol Scand*, 76 (6): 555-558.