

# Laparoscopic Ovarian Drilling by Diathermy for Ovulation Induction in Infertile Women with Polycystic Ovarian Syndrome

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## Abstract

**Background:** Polycystic ovarian syndrome (PCOS) is the commonest cause of secondary infertility. Laparoscopic ovarian drilling has widely been used for induction of ovulation in polycystic ovarian syndrome patients resistant to clomiphene citrate. 80% patients ovulated after treatment and 60% patient conceived either spontaneously or after treatment with medication to which they are previously resistant.

**Purpose:** The aim of the present study was to see the effectiveness of laparoscopic ovarian drilling (LOD) with monopolar diathermy on pregnancy outcome in infertile women with polycystic ovarian syndrome (PCOS).

**Design:** Descriptive cross sectional study.

**Intervention:** Laparoscopic ovarian drilling.

**Main Outcome Measures:** Pregnancy, ovulation rate.

**Material and Methods:** This study was carried out in the department of Gynae and Obstetrics in Sharif Medical City Hospital from January, 2007 to January, 2009. The inclusion criteria for laparoscopy ovarian drilling (LOD) were those infertile women between the age group of 25 – 38 years who meet the criteria for PCOS and who are resistant to clomiphene citrate and injectable gonadotrophins. A total of 30 women were booked for laparoscopic ovarian drilling after having informed consent for procedure. Response to therapy was assessed in term of pregnancy outcome and ovulation rate for 1 year after therapy.

**Results:** A total of 30 patients were booked for laparoscopic ovarian drilling from January, 2007 to January, 2009. The mean age of study group was 30 years  $\pm$  SD 4.7791. Cumulative ovulation rate was observed in 22 patients (73%), out of which spontaneous ovulation occurred in 18 patients (80%), and after ovulation induction therapy in 4 patients (18%). Eleven patients (37%) conceived in two year duration. Spontaneous conception without any treatment was observed in 7 patients (63%); however 4 patients (37%) require further assistance with combined therapy of clomiphene citrate and injectable gonadotrophins after failure of ovulation induction. Miscarriage occurred in none of our patients. Mean age of conceived group was 29.36  $\pm$  SD 5.07 years; with mean duration of infertility 5.136  $\pm$  SD 4.605 years. Most of the patients conceived in first 4 months of LOD i.e 8 patients (72%), two patients (18%) in further 8 months, and 1 patient in 1 year duration. Mean interval of conception was 3.95  $\pm$  SD 4.14 months after laparoscopic ovarian drilling. None of our patient lost follow up.

**Conclusion:** Laparoscopic ovarian drilling is safe, cost effective treatment in patients with polycystic ovarian syndrome. Spontaneous ovulations were observed within 2 – 3 months, and maximum conception occurred in 6 to 9 months of treatment with LOD.

**Key Words:** PCOS, Laparoscopy.

## Introduction

Polycystic ovarian syndrome (PCOS) is associated with chronic anovulation and infertility. In most cases ovulation can be induced with clomiphene citrate (CC) but approximately 25% of patients fail to ovulate and require alternative treatment. Human menopausal

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gonadotrophins have been used but the risk of hyperstimulation and multifetal gestations are high. A variety of surgical option laparoscopic ovarian drilling (LOD) proposed by Gjonness in 1984 has now widely been accepted as a second – line treatment for anovulatory infertility due to polycystic ovary syndrome (PCOS). This approach not only produces high ovulation and pregnancy rates but also corrects the endocrine abnormalities associated with this syndrome.<sup>1</sup>

Gjonness with his multi electro cauterization in polycystic ovarian disease (PCOD) achieved an ovulation rate of 92% and pregnancy rate of 69% and miscarriage rate of 15%. He postulated that ovulation is either by non-specific stromal cause or extensive capsular destruction with the discharge of contents of a number of follicular cysts or the local capsule of one specific but unidentified capsule.<sup>2</sup>

Other postulated mechanism is, after ovarian surgery in PCOS, a rapid reduction in serum levels of all ovarian hormones, in combination with increased serum levels of pituitary hormones. Continuation of follicle growth in subsequent cycles after ovarian surgery occurs in an environment with less androgens and lower LH and FSH levels compared with pretreatment levels. Additionally, anti – Mullerian hormone and gonadotrophin surge attenuating factor probably have role in the endocrine changes.

An analysis of the first 35 reports, mostly uncontrolled series, showed that 82% of 947 patients ovulated following the operation and 63% conceived either spontaneously or after treatment with medications to which they had previously been resistant. A Cochrane data base analysis of six randomized controlled trials mostly comparing laparoscopic ovarian drilling with gonadotrophin therapy, showed similar cumulative ongoing pregnancy rates 6 – 12 months after LOD and after 3 – 6 cycles of gonadotrophin therapy. If ovulation is not forthcoming within 2 – 3 months following LOD, then ovulation induction can often be more successfully employed than preceding the operation.<sup>3,5</sup>

With laparoscopic surgery, in addition to a very high prevalence of monofollicular ovulation, there is decrease risk of ovarian hyperstimulation (OHSS) and multiple pregnancies and occurrence of consecutive ovulations without the need for further treatment, and safety; while the disadvantages are the need for a surgical procedure and creation of tubo-ovarian adhesions. It has been found that cost of a live birth was one third lower in the group that underwent laparoscopic ovarian diathermy as compared to those who received

gonadotrophins therapy for ovulation induction.<sup>4,6</sup>

Despite LOD, 20 to 30% of anovulatory PCOS women fail to respond to this therapy. It may be due to the amount of LOD is not sufficient to produce an effect in patients or inherent resistance. Therefore in order to improve success rate, predictors of success must be identified. The predictors of success of LOD include body mass index, serum testosterone concentration, free androgen index and duration of infertility.<sup>7</sup>

The aim of present study was to see the clinical outcome and effectiveness after laparoscopic ovarian drilling using bilateral diathermy on ovaries in terms of ovulation and pregnancy rate.

## Material and Methods

### Inclusion Criteria

This study was carried out in the department of Gynae and Obstetrics Sharif Medical city Hospital from January, 2007 to January, 2009. The inclusion criteria for laparoscopy ovarian drilling were those infertile women between the age group of 25 – 38 years who meet the criteria for polycystic ovarian syndrome. The presences of at least two of the following criteria are required for confirmation of PCOS.

1. Menstrual irregularities and anovulation.
2. Clinical and biochemical evidence of hyper androgenaemia.
3. Presence of characteristics of polycystic ovarian syndrome on ultrasound examination.
4. Elevated leutenizing hormone (LH) or L H: FSH ratio > 2.

The patients who are booked had already received 6 month trial of ovulation induction therapy with combined oral clomiphene citrate CC (150 mg / day) from 2<sup>nd</sup> to 6<sup>th</sup> day of cycle and injectable gonadotrophins therapy from day 6<sup>th</sup> to 10<sup>th</sup> of menstrual cycle and are resistant to treatment. Failure of ovulation was confirmed on ultrasound and by low day 21 serum progesterone levels (< 30 nmol/l). Patients were enrolled after having informed consent. Detailed history was taken regarding menstrual irregularities (oligo or amenorrhea), hirsutism, and obesity, type of infertility (primary or secondary) and duration of infertility. Detail examination was done including body weight, height in meters, hirsutism and galactorrhea. Body mass index was calculated using formula weight in Kg/height in meter.<sup>2</sup> Pelvic examination was performed to exclude any other pathology. Transvaginal ultrasound was done to confirm the diagnosis of polycystic ovaries on

ultrasound (ovarian stromal hypertrophy and multiple small 6 – 8 follicles arranged in periphery). Normal husband semen analysis and patent fallopian tubes was a prerequisite for laparoscopic ovarian drilling. All women undergo hormonal analysis including day 3 S. FSH, S. LH, S. LH / FSH ratio, S. TSH and, S. Prolactin levels.

**Exclusion Criteria**

The exclusion criteria were other endocrinological abnormalities such as hyperprolactinaemia, and thyroid dysfunction.

**Laparoscopic Ovarian Drilling**

A total of 30 women were booked for laparoscopic ovarian drilling after having informed consent. Lapa-

roscopy was done under general anesthesia .The pneumo peritoneum was created with veress needles. 10 mm infra umbilical port and two 5 mm lateral ports in lower abdomen just above the anterior superior iliac spine lateral to inferior epigastric vessels were inserted. The laparoscope introduced through the infra umbilical port and ancillary ports were placed after charting the vessels by trans-illumination. Inspection of the pelvis was carried out to rule out other factors of infertility. A good uterine manipulator was used to stretch the ovarian ligament. The ovary was lifted by suction cannula and placed over the cervico-uterine junction which forms a platform and easy to carry out the puncture. The mono polar needle was introduced at right angle to the ovary avoiding injury to the hilum. 30 watts current was used making 4 – 6 holes each lasting 4 sec at a depth of 3 – 4 mm to both ovaries. A thorough suction irrigation was done afterward. Hydro-

**Table 1:** Demographic Features of Study Group n = 30.

Characteristics	No of Patients	% age
Age		
25 – 30	20	67%
31 – 35	7	23%
36 – 38	3	10%
Mean age : 30 year STD ± 4.7791		
Duration of Infertility		
2 – 5 years	18	60%
5 – 10 years	6	20%
> 10 years	6	20%
Mean duration of infertility: 6.2 years STD ± 4.0915		
Type of Infertility		
Primray	12	40%
Secondary	18	60%
Body Mass Index		
BMI < 25 kg/m <sup>2</sup>	12	40%
BMI > 25 kg/m <sup>2</sup>	18	60%
Hirsuitism		
Yes	16	53%
No	14	47%
Menstrual Pattern		
Oligoamenorrhoea	20	67%
Amenorrhoea	6	20%
Regular cycle	4	13%
Hormonal Profile		
S LH / FSH ratio (Normal)	11	36.7%
S LH / FSH ratio > 2	19	63.3%

Menstrual pattern definition: regular cycles = cycle length between 25 and 35 days; oligomenorrhoea = cycle length between 35 days and 6 months; amenorrhoea = absence of the menstrual period for > 6 months.

flotation with 500 ml ringer lactate will be done which minimize postoperative adhesion.

### Postoperative Monitoring

The following outcome measures were collected and reported for 1 year. After the first spontaneous menstruation, ovulation rate was determined by day 21 serum progesterone levels of  $> 30$  nmol/l. If the patient did not ovulate as evidenced by the low progesterone levels or lack of menstruation clomiphene citrate (CC) and injectable gonadotrophins would be started again 6–8 weeks after surgery. If ovulation was achieved either spontaneously or with the help of CC, patients were followed-up until they conceived for up to 12 months after LOD.

### Statistical Analysis

The statistical analysis was carried out using Chi Square for association between variables using SPSS 11 version of window. The P value of  $< 0.05$  was used as the cut off level for significance. Variables are described by frequencies and mean  $\pm$  standard deviation (SD).

### Results

This study was carried out in the department of Gynae and Obstetrics of Sharif Medical City hospital in 2 – year duration from January, 2007 to January, 2009. A total of 30 patients were booked for laparoscopic ovarian drilling after failure of combined therapy of clomiphene citrate and injectable gonadotrophins for ovulation induction. An informed consent was taken from all patients about the procedure. The demographic characteristics of booked patients were as follows. The patients booked were in the age group of 25 – 38 years. The mean age of patients was 30 years  $\pm$  SD 4.779. Eighteen patients (60%) had BMI  $> 25$  kg/m<sup>2</sup>, while 12 patients (40%) had BMI index of  $< 25$  kg/m<sup>2</sup>. Hirsutism was observed in 16 patients (53%). As far as menstrual irregularities were concerned 20 patients (67%) had oligoamenorrhea, 6 patients (20%) had amenorrhea while 4 patients (13%) had regular cycles. Among 30 patients, 12 patients (40%) suffered from primary infertility, 18 patients (60%) with secondary infertility. Most of the patients with secondary infertility had high miscarriage rate due to high LH /

FSH ratio. Biochemical analysis shows that 19 patients (63%) had high LH / FSH ratio of  $> 2$  while 11 patients (37%) had normal levels. As far as duration of infertility is concerned 18 patients (60%) had  $< 5$  year duration of infertility, 6 patients (20%) between (5 – 10 year duration), and 6 patients (20%) had  $> 10$  year duration of infertility. The mean duration of infertility was 6.2 years  $\pm$  SD 4.0915 (Table 1).

In 1 year of follow up, 11 patients (37%) conceived out of 30. The mean age of conceived group was 29.36  $\pm$  SD 5.071 years (TABLE 5). Out of 30 patients, spontaneous ovulation was observed in 18 (82%) while another 4 patients (18%) ovulated in response to further treatment of gonadotrophins and clomiphene citrate so cumulative ovulation rate of 73% was observed. Spontaneous conception was observed in 7 patients (63%) while 4 patients (37%) require further assistance in the form of combined CC and injectable gonadotrophins so cumulative conception rate of 37% was observed (Table 2 and 3).

**Table 2:** Clinical Outcome: N = 30.

Outcome	No of Patients	% age
Cumulative Ovulation	22	73%
Cumulative conception	11	37%

**Table 3:** Follow-up of Clinical Outcome.

Follow up	Spontaneous	After Ovulation Induction Therapy
Ovulation n = 22	18 (82%)	4 (18%)
Pregnancy n = 11	7 (63%)	4 (37%)

**Table 4:** Interval between Conception and Ovarian Drilling.

Interval	No	Percentage
1 – 4 months	8	73%
5 – 8 months	2	18%
9 – 12 months	1	9%

Mean duration of interval: 3.954  $\pm$  SD 4.140 months

Among 11 conceived patients, 9 patients (82%) had live birth, while 2 patients (18%) had ongoing pregnancy while none of our patient abort after

laparoscopic ovarian drilling suggesting decrease LH level after LOD.

Most of the patients conceived in first 4 months of LOD i.e 8 patients (72%), two patients (18%) in further 8 months, and 1 patient in 1 year duration. The mean interval of conception and ovarian drilling was  $3.95 \pm SD 4.140$  months (Table 4).

The predictors of success were also identified among conceived group when compared to women who were not conceived. The mean age of conceived group was  $29.36 \pm SD5.071$  years ( $P 0.8502$ ). The mean duration of infertility was  $5.136 \pm SD 4.650$  years. Five patients who conceived had  $< 5$  year of duration of infertility while 3 patients between (5 – 10 years), and 3 patients had  $> 10$  year of duration of infertility suggesting the fact that conception was higher in women who had lesser duration of infertility. ( $P 0.465$ ) These findings are consistent with our earlier report (Li *et al.*, 1998) which showed that women with a duration of infertility  $> 3$  years were less likely to respond to LOD. A possible explanation for this is that women with longer duration of infertility are more likely to have other subtle subfertility factors.

Most of the patients who conceived had secondary infertility ( $P 0.278$ ), and had BMI  $< 25 \text{ Kg/m}^2$  ( $P .0444$ ). The results confirm that women with marked obesity (BMI  $> 25 \text{ kg/m}^2$ ) achieved significantly lower ovulation and pregnancy rates compared with those  $< 25 \text{ kg/m}^2$  women. None of our patient lost follow up and had multiple pregnancy.

## Discussion

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age The prevalence of this syndrome is approximately 6%. Infertility due to ovulatory dysfunction is a common problem for women with PCOS. The optimal management of PCOS is uncertain, but treatment focuses on amelioration of the chemical features. For the most part, treatment aims to restore ovulatory cycles so that pregnancy can be achieved. It has now been recognized that laparoscopic ovarian drilling (LOD) is an effective second – line treatment for CC – resistant anovulatory infertility associated with PCOS.<sup>1</sup>

Gjonnaess reported an ovulation rate of 92% and a pregnancy rate of 70% after laparoscopic ovarian electrocoagulation in patients with PCOS. This was the spark that reignited interest in surgical management of the disease and heralded the era of minimally invasive surgery in the treatment of these patients. Following this report, several studies described the success and utility of this procedure, with ovulation rates ranging from 64% to 92% and pregnancy rates from 41% to 80%. Our results in this study are encouraging both in terms of the initiation and persistence of regular ovulatory cycles and in terms of pregnancies.<sup>2</sup>

All our patients who were booked for LOD had previously been treated unsuccessfully with CC and several had HMG treatments. In this study out of 30 patients who underwent LOD; cumulative ovulation

**Table 5:** Characteristics of Women Who Conceived n = 11.

Variables	N = 30	Conceived Group n = 11	P value
AGE (years)			
25 – 30	20	8	0.8502
31 – 35	7	2	
36 – 38	3	1	
Mean age: 29.36 years $\pm$ SD 5.071			
Infertility			
Primary	12	3	
Secondary	18	8	
Duration of Infertility			
2 – 5 years			0.4651
6 – 10 years	18	8	
> 10 years	6	2	
	6	1	
Mean duration: 5.136 $\pm$ SD4.650			
BMI			
< 25 kg/m <sup>2</sup>	12	7	.0444
> 25 kg/m <sup>2</sup>	18	4	

P value  $< .05$  statistically significant

rate was 73.33%. Spontaneous ovulation was observed in 18 patients (82%) while 4 patients (18%) require further assistance in form of combined clomiphene citrate and gonadotrophins for ovulation. The results are comparable to study conducted by S.A.K. Amer, T.C. Li and W.L. Ledge in which overall ovulation rate was 78% out of which 57% ovulated spontaneously and further 43 patients ovulated after addition of CC and gonadotrophins. Ultrasonography and day 21 serum progesterone levels confirmed ovulation.<sup>3</sup> Our results validate those of similar earlier reports and confirmed the notion that laparoscopic ovarian drilling increases the sensitivity of the ovaries to CC and gonadotrophins. It is also associated with higher ovulation and pregnancy rates, while reducing the dosage and duration of HMG treatment together with the reduction in the incidence of ovarian hyperstimulation in such patients.

As far as pregnancy outcome was observed cumulative conception rate was 37% with a live birth rate of 81%, 2 patients (18%) had ongoing pregnancies and none of our patient had miscarriage. The results are comparable to study by Mahmoud N. Abdul Salam, Fathia H. Hasanain, Bothina K. Greiew and Soliman et al in which the pregnancy rate of 38% was observed.<sup>5</sup>

Spontaneous conception was observed 63.63% while 4 patients (37%) require further therapy of gonadotrophins although the dose of gonadotrophins for ovulation was significantly reduce in comparison to dose required prior to treatment with LOD. The results are comparable to Farhi. et al who performed a study to evaluate the effect of ovarian electro cauterization and ovarian response to gonadotrophin stimulation and pregnancy rate in clomiphene citrate resistant PCOS.<sup>6</sup> Comparison of gonadotrophins stimulated cycle before and after electro cauterization revealed higher rates of ovulation and pregnancy after surgery as well as significant reduction of gonadotrophin ampoules.

In our study about 63.33% were still resistant to treatment and low pregnancy rate despite high ovulation rate were observed. A possible explanation is that the amount of ovarian tissue destroyed during LOD is not sufficient to produce an effect or inherent resistance of ovary to the effect of ovarian drilling. Another cause may be hyper prolactaemia observed in some patients after LOD. Therefore it is important to monitor the patients for prolactin levels after LOD. The drawback with LOD is to quantify the dose of diathermy to a particular patient. It is difficult to decide the dose for a particular patient with out knowing the dose response. There is a need to optimize the dose of LOD in

response to ovarian size.<sup>8</sup>

It was reported that the beneficial effects of the surgical treatments are of limited duration, in most studies up to one year. However, pregnancies have been known to occur after 12 months and in our study most of the patients conceived in first 4 months of LOD. The mean interval of conception and LOD was  $3.954 \pm SD 4.140$ , i.e 8 patients (72%), two patients (18%) in further 8 months, and 1 patient in 1 year duration as we limited our study to 1 year duration of follow up. The results are comparable to study by Eftekhar Hassan in which most conceptions 80% occurred in the first year after surgery, (11%) patients conceived in the first 6 months of the next year and the remaining (3.9%) conceived in the second half of the next year after drilling.<sup>9</sup>

In this study most of the patients who underwent LOD had LH / FSH ratio of  $> 2$  (63%) while 37% had normal ratio. LOD reduces serum concentration of LH and LH / FSH ratio in follow up period. In a study by S.A.K.S. Amer,<sup>1</sup> Z. Banu, T.C. Li and I.D. Cooke the serum concentrations of LH and the LH: FSH ratio decreased significantly after LOD and remained low during the medium – and long – term follow-up. Women with high LH concentrations ( $> 10$  IU/l) before and after LOD showed a significant ( $P < 0.01$ ) decrease from 70% prior to LOD to 33% shortly after surgery But the proportion remained low during the medium – and long – term follow-up periods (45 and 31%). The results are comparable to our study in which most of the patients conceived in first four months of follow up. As LH levels falls spontaneous ovulation and conception rate increase although in our study we did not do LH levels afterwards.<sup>4</sup>

The predictors of success of LOD depends on the body mass index, serum testosterone concentration, free androgen index and duration of infertility, these predictors will help in selection of cases for LOD. When predictors of success was found in study group, most the patients who conceived were  $< 30$  years of age (mean age  $29.36 \pm SD5.07$  years), had  $< 5$  year duration of infertility (mean duration  $5.136 \pm SD4.650$  years), suffers from secondary infertility and had BMI of  $< 25$  KG/m<sup>2</sup> ( $P .0444$  statistically significant) (Table 5).

There were no multiple pregnancies observed in the study group. Similarly, according to the other studies, multiple pregnancy rates are reduced in those women who conceive following laparoscopic drilling compared with this rate in gonadotrophin therapy.<sup>2</sup>

In this study we used diathermy for bilateral

ovarian drilling. Gadire.al regards the laparoscopic cauterization of ovaries to be most effective treatment for PCOS. The ovulation rates were higher in electrocauterization group. In another study by Kovacs treated patients with PCOS with electro cauterization at separate points on each ovary and found that 70% of women ovulated and 20% became pregnant so the results are comparable to our study in term of ovulation and pregnancy outcome.<sup>7,8</sup>

There was no complication observed in study group.

### Conclusion

Laparoscopic ovarian drilling using diathermy is an effective treatment modality in PCOS patients resistant to clomiphene citrate. It not only results in high ovulation and conception rate without major complications but also the duration of effect lasts for 1 year after this therapy.

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