RESEARCH ARTICLE

Surgical Treatment for Polycystic Ovary Syndrome and Reproductive Outcomes: A Retrospective Study

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Abstract

Aim: To assess the reproductive outcome after ovarian drilling by laparoscopic technique, and also to analyze a number of penetrations per ovary to improve the ART outcome.

Materials and methods: A retrospective study was performed at Sudha Hospital and Research Institute, Erode, Tamil Nadu over a period from January 2018 to December 2020. This study includes 254 infertile women with polycystic ovary syndrome (PCOS) and clomiphene–citrate resistance, who were subjected to ovarian drilling by laparoscopy using a drilling needle. Patients are divided into 2 groups, 1st group had less than 4 penetrations per ovary and 2nd group had above 4 penetrations per ovary. The results elicited from both the groups were compared.

Results: The 2 groups did not show any significant difference about body mass index (BMI), insulin, and glucose levels before and after the procedure. The confirmed pregnancy was 79.2% in the group with 4 punctures and it was 74.6% in the group with more than 4 punctures. The miscarriage rate was 8.1% and 13.9% in the group with punctures less than 4 and more than 4 respectively. Significant improvement (p-value = 0.029) in live birth rate (70.3%) was observed in the group with less than 4 punctures.

Conclusion: Ovarian drilling is a successful treatment in patients with clomiphene citrate-resistant PCOS. A remarkable improvement was observed in the confirmed pregnancy rate in patients who were subjected to ovarian drilling. It was observed that 4 penetrations per ovary were adequate to increase the outcome in comparison to more than 4 punctures per ovary.

Keywords: Clomiphene citrate resistant, Ovarian drilling, Polycystic ovary syndrome.

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Introduction

Polycystic ovary syndrome (PCOS) is one of the most frequent endocrine disorders in the reproductive age which affects about 5–10% of women.[1] The common presentation of this syndrome includes menstrual problems, hirsutism, and chronic anovulation all associated with hyperandrogenic state. Patients with this syndrome are at higher risk of developing obesity, insulin resistance, dyslipidemia, infertility, cardiovascular disorder, and endometrial cancer. Polycystic ovary syndrome is characterized by anovulation due to development defects in follicles beyond 10mm in size. The treatment proposed for women with PCOS is always debatable. Various treatment options have been proposed like lifestyle modification, administration of drugs, ovarian drilling by laparoscopy, and assisted reproductive technique (ART). The ovulation and pregnancy rates were 80–40% respectively, in women using clomiphene as first-line treatment for ovulation induction, about 15–20% have anovulation even with a maximum dose of clomiphene citrate (CC).[2] Clomiphene citrate resistant patients were given gonadotropins as first-line management and the recommended second-line intervention is laparoscopic ovarian surgery (LOS).[1]

The surgical approach to induction of ovulation started with wedge resection to modern-day ovarian drilling. The most common indication is for the CC-resistant women with anovulation, persistent raised LH, or women with severe PCOS who require strict monitoring during high-dose gonadotropins for induction of ovulation. Laparoscopic ovarian surgery alone is beneficial in <50% of women and additional ovulation induction drugs are essential for those patients.[3] Laparoscopic ovarian surgery procedure includes a number of punctures for each ovary and it varies from 4 to 40 punctures per ovary. It is suggested that the degree of thermal injury must be decided by the ovarian size and stroma. Most authors use 4 to 10 punctures, but the more punctures there are, the higher the chances of ovarian failure rates. Laparoscopic ovarian surgery can achieve mono follicular ovulation with minimal risk of ovarian

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hyper-stimulation. The risks include adhesions, pelvic abscess, and destruction of ovarian tissue leading to loss of ovarian function. This retrospective study was conducted to assess the effect of reproductive outcomes in patients with PCOS with LOS and also to evaluate a number of punctures per ovary for the effective outcome.

Materials and Methods

Study Design

A retrospective study was performed at Sudha Hospital and Research Institute, Erode, Tamil Nadu over a period from January 2018 to December 2020. This study includes 254 infertile women with PCOS and clomiphene–citrate resistance, who were subjected to ovarian drilling using a laparoscopic drilling needle. Inclusion criteria: Age <35, infertility >2 years, BMI <32 kg/m^2, normal semen analysis, and presence of clomiphene citrate resistance (failure to ovulate with 200 mg of cc from day 2 to 6 for at least 3 consecutive cycles).

A detailed history regarding the age, infertility period, menstrual history, and previous history of ovulation induction are collected. Their BMI is calculated. A complete hormone profile is done for all patients. Women were then offered lifestyle modification. These patients are then subjected to LOS and divided into 2 Groups. The procedure included immobilization of the ovary, 40 watts coagulation with complete insertion of a needle into the stroma of the ovary. Group I had 4 penetrations per ovary and 2nd Group had more than 4 penetrations per ovary. Ovaries are washed with normal saline. If spontaneous pregnancy was not achieved within 3 months of LOS, gonadotropins were started for ovulation induction and followed for a further 6 months. Confirmed pregnancy was defined as the presence of a gestational sac in ultrasonography.

Data Validation

The reliability of the PCOS was evaluated by internal constancy and test-retest reliability. The method of Kuder Richardson 20 (KR-20) reliability and Cronbach's alpha coefficient was deliberated for 3 point scaling variables on a scale of 1–3 (mild, moderate, and severe) respectively. Similarly, Cronbach's alpha coefficient indicates adequate reliability for a group of questions related to the approach to PCOS ($\propto = 0.84$).

Data and Statistical Analysis

Data is entered manually in Microsoft Excel and exported to SPSS version 26.0 for statistical analysis. Categorical variables are presented as frequency tables, and continuous variables are presented as descriptive measurements, expressed as mean and standard deviation. Odds ratios were used to test the association between exposure and the outcome of the binary variable. For all analyses, a *p*-value of less than 0.05 and a 95% confidence interval that does not spread uniformity were considered as thresholds to be the gateway to statistical significance.

Model for Adoption

The association between AMH, prolactin, estradiol, and endometrial thickness provided by box and whisker plot analysis for predicting clinical pregnancy rate. The box and whisker plot analysis was performed using the software IBM SPSS version 26.0. To estimate the overall accuracy, including the entire range of probable thresholds, we expected the number summary statistics in a visually appealing and interpretable way is introduced in this section "minimum", first quartile (FQ1), median, third quartile (TQ3), and "maximum". The distance between the upper and lower quartiles of the data sets,

$$IQR = TQ_3 - FQ_1 = q_n(0.75) - q_n(0.25)$$

The change of informative infertility maps harmonizes box plot statistical analysis of spatial variation and for their recipient of the information much more than the associated statistics. Boxplot comparison of approximate normal distribution and probability density function for normal distribution. The formula below is the probability density function for a normal distribution.

$$f\left(x/\mu,\sigma^2\right) = \frac{1}{\sqrt{2\pi\sigma^2}}\, e^{-\frac{(x-\mu)^2}{\sigma^2}}$$

Let us simplify it by assuming we have an average or mean (μ) of 0 and a standard deviation (σ) of 1.

$$f(x) = \frac{1}{\sqrt{2\pi}}\, e^{-\frac{x^2}{2}}$$

It should be noted that for any probability density function, the area under the curve should be 1.

$$\int_{-\infty}^{\infty} = \frac{1}{\sqrt{2\pi}}\, e^{-\frac{x^2}{2}dx}$$

Where ∞ denotes the pregnant, −∞ denotes the non-pregnant, denotes the hormonal variables impact on pregnancy outcomes, and denotes the constant variable.

Table 1: Baseline characteristics in polycystic ovaries and ART outcomes in pregnant and non-pregnant group

Variables	*Pregnant (198)*	*Non-pregnant (56)*	*p-value*
Age	29.24 ± 5.37	29.25 ± 3.81	0.678
BMI	27.18 ± 4.10	27.36 ± 5.48	0.242
Duration of infertility			
Below 5 years	95 (48.0)	22 (39.3)	
6–10 years	76 (38.4)	17 (30.4)	0.767
11–15 years	18 (09.1)	10 (17.8)	
Above 20 years	9 (4.0)	7 (12.5)	
Type of infertility			
Primary infertility	145 (73.2)	45 (80.4)	0.679
Secondary infertility	53 (26.8)	11 (19.6)	
Menstruation			
Regular	53 (26.8)	8 (14.3)	0.026**
Irregular	145 (73.2)	48 (85.7)	

*Significant at the 0.01 level; **Significant at the 0.05 level

Results

Table 1 shows the demographic details, and comparison done between the pregnant and non-pregnant members. There was no significant difference between age and BMI. Most of them had primary infertility with less than 10 years of infertility. The most common menstrual disorder was an irregular menstrual cycle.

Table 2 compares the biochemical and hormonal values between the two groups. There was a significant reduction in the AMH and LH values in the group with more than 4 punctures. Not much difference in FSH, prolactin, and TSH values.

Table 2: Hormonal and reproductive data of both groups after laparoscopic ovarian drilling

Variables	*Below 4 puncture*	*Above 4 puncture*	*p-value*
AMH	5.58 ± 3.73	3.96 ± 2.56	0.001*
TSH	3.15 ± 2.69	3.29 ± 4.72	0.763
FSH	9.35 ± 19.25	7.52 ± 5.60	0.652
LH	10.60 ± 12.59	7.46 ±4.47	0.266
Prolactin	16.83 ± 10.78	16.03 ± 10.55	0.042**
Estradiol	91.09 ± 130.45	122.00 ± 127.77	0.034**
Endometrial Thickness	0.91 ± 0.27	0.94 ± 0.25	0.040**

*Significant at the 0.01 level; **Significant at the 0.05 level

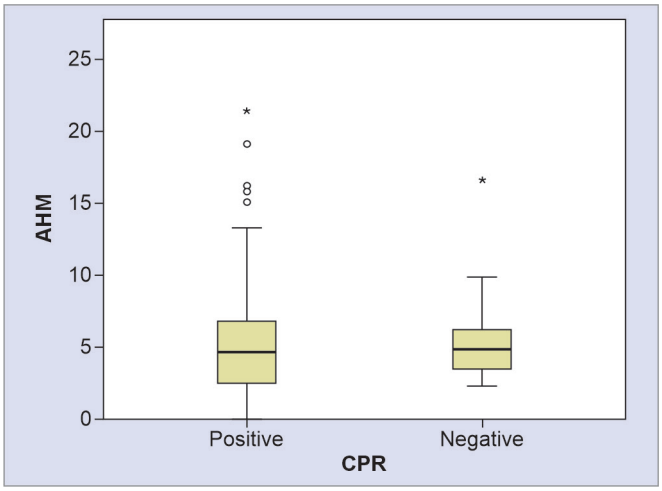

Fig. 1: Diagnostic limits of maximum AMH given by box plot analysis for predicting clinical pregnancy rate

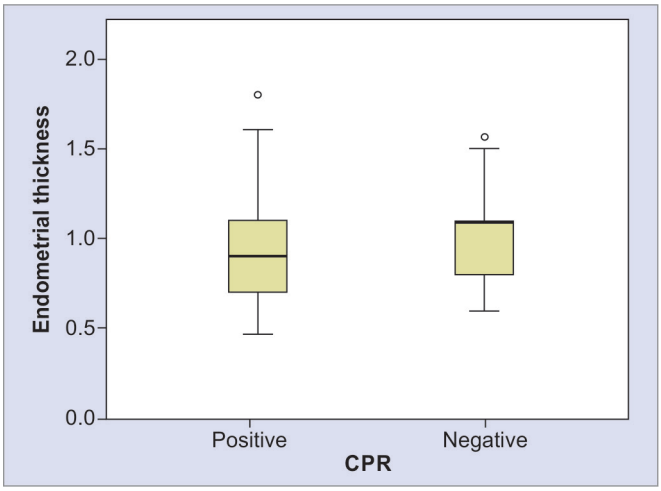

Fig. 2: Diagnostic limits of maximum endometrial thickness given by box plot analysis for predicting clinical pregnancy rate

In Figures 1 and 2, the diagnostic thresholds of maximal AMH and endometrial thickness prediction of clinical pregnancy rate the box plot is symmetrical, it defines that our data follow a normal distribution. In Figures 3 and 4, the diagnostic threshold of maximal prolactin and estradiol prediction of clinical pregnancy rate the box plot is symmetrical, it defines that our data follow a normal

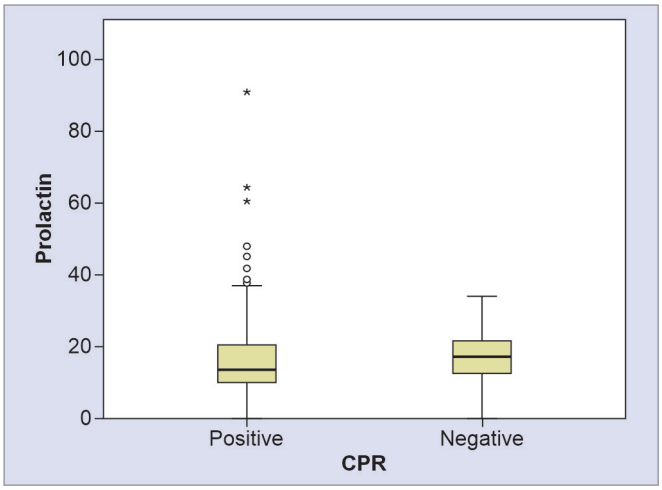

Fig. 3: Diagnostic limits of maximum prolactin given by box plot analysis for predicting clinical pregnancy rate

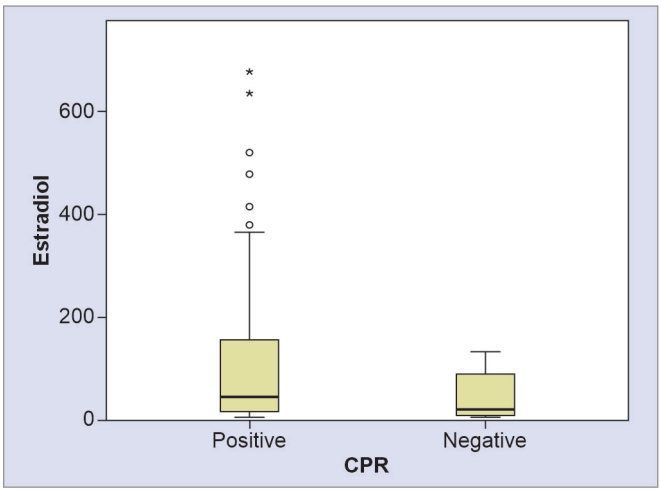

Fig. 4: Diagnostic limits of maximum estradiol given by box plot analysis for predicting clinical pregnancy rate

distribution positively skew. The boxes are all above the line marked a positive association may exist between pregnancy outcome and hormonal variables. The boxes move upward as the pregnancy outcome improves. This shift suggests that specially designed this study generally finds stronger associations between pregnancy outcome and hormonal variables.

Table 3 shows the reproductive outcome between the group with below 4 punctures per ovary and above 4 punctures per ovary. The clinical pregnancy rate was 79.2% in group I and it was 74.6% in group II with *p*-value of 0.021. It was observed that miscarriage rates were less in a group with 4 punctures per ovary (8.1%) compared to another group (13.9%) with a significant *p*-value (0.043). the live birth rate was 70.3% in group I and 67.7% in group II with a significant *p*-value (0.029). The on-going pregnancy rate was also high in the group with 4 punctures per ovary (21.6%) with a significant *p*-value (0.011).

Discussion

There are very few studies to compare the effectiveness of laparoscopic ovarian surgery (LOS) in CC-resistant PCOS. Few studies

Table 3: Comparison of reproductive outcomes for both groups

Parameters	*Below 4 puncture*	*Above 4 puncture*	*p-value*
Clinical pregnancy rate *n* (%)	61/77 79.2%	132/177 74.6%	0.021**
Miscarriage rate/pregnancy *n* (%)	6/74 8.1%	22/58 13.9%	0.043**
Live birth rate *n* (%)	52/74 70.3%	107/158 67.7%	0.029**
Ongoing pregnancy	16/74 21.6%	21/158 18.4%	0.011**

**Significant at the 0.05 level

used upto 4–40 punctures per ovary.[4] In the majority of studies, more than 10 punctures were used.[5] The thermal injury to ovarian tissue results in a reduction in the serum androgen levels, reducing the peripheral aromatization to estrogen. This restores the feedback mechanism resulting in follicular development and ovulation with gonadotropin stimulation.[5]

Our study showed a clinical pregnancy rate between 79.2% and 74.6% in groups I and II respectively. The results were more when compared to other studies and also showed that 4 punctures per ovary are sufficient to give an effective outcome compared to the group with more punctures. Similar results were observed in a study done by Thomas and Michaedl.[6] Study done by Poonam et al.[7] showed pregnancy rate after 6 cycles of gonadotropins were 45.45% and it was 40% after the LOD group. The discrepancy with other studies could be due to many factors such as duration of infertility, follow-up period, and drugs used for induction of ovulation. Most of the patients in our study had less than 10 years of infertility; many underwent IVF procedures due to other factors like male factor infertility. Moreover, the period of follow-up was 6 months in our study compared to some studies with long periods of follow-up. Thus, it proves that younger women with fewer period of infertility with cc resistance had better reproductive outcomes.

Miscarriage affects around 30–50% of patients with PCOS.[8] This rate was significantly reduced after laparoscopic ovarian drilling. The miscarriage rate was 8.1% and 13.9% in the group with 4 punctures per ovary and 8 per ovary respectively in our study. Similar results were observed in a study done by Hasan and Qublan HS[2] with 12.5–15.4% in 5 and 10 punctures per ovary. Similar results with Srivastava et al.[9] with miscarriage rate of 6% in the LOD group. Reduction in miscarriage rates is due to normalisation of hormone milieu which improves both endometrium and embryo for implantation.

Laparoscopic ovarian drilling has few serious complications like postoperative adhesions that result in severe abdominal pain, bowel obstruction, and rarely tubal adhesion and infertility.[10] In our study, we did not come across any complication after laparoscopic ovarian drilling. This must be due to the use of the insulated laparoscopic drilling needle which will minimize the thermal injury to the ovarian tissue and also thorough saline wash after drilling causing less or rather nil complications. Another complication was premature ovarian failure which was also not encountered in our study.

Conclusion

Laparoscopic ovarian surgery is a very effective treatment in CC-resistant PCOS women. The confirmed pregnancy rate and the live birth rate significantly increased in women who underwent LOS. It was observed that a minimal 4 penetrations per ovary are sufficient to produce an effective reproductive outcome when compared to the Group with a larger punctures per ovary. Further studies are required with more sample size and a long period of follow-up to second these results.

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