ORIGINAL ARTICLE

Laparoscopic Ovarian Drilling for Achieving Pregnancy among Women with Polycystic Ovarian Syndrome

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Abstract

Background: Infertility is a critical and emotionally challenging issue for reproductive-age couples, affecting their physical and mental well-being. World Health Organization (WHO) has highlighted that approximately 25% of couples in developing countries are unable to conceive, attributing infertility to a combination of biological, environmental, and lifestyle factors.

Objective: The study aimed to evaluate laparoscopic ovarian drilling for achieving pregnancy among women with polycystic ovarian syndrome, resistant to clomiphene citrate.

Methodology: This retrospective chart review was conducted on secondary data to identify the effect of ovarian drilling on clients with PCOS who were resistant to Clomiphene Citrate and were unable to conceive before the drilling procedure. Data was retrieved from the case files of 133 couples available with the hospital's data bank for the past four years (Jan 2016 to Dec 2019) by a non-probability consecutive sampling of women resistant to clomiphene citrate with PCOS. The place of study was the Australian Concept Infertility Medical Center, Clifton, Karachi.

Results: A total of 133 patients were enrolled in the study; the mean age was 28.94±4.97 years, 70% suffering from primary infertility while 30% were from secondary infertility. Pregnancy outcome was reported as Pregnancy and/or ovulation 89 % and no response 11%. The study outcome was associated with determinants including FSH levels, LH levels, Prolactin levels and TSH levels respectively. The Odds of negative response to ovarian drilling were reported with FSH value of <5-7 with OR of 18.8 and CI 95% of 2.97-119.9, LH value of <5-7 with OR of 0.395, CI 95% of 0.063-2.46, Prolactin of <5-15 with OR of 0.285 and CI 95% of 0.050-1.63 while TSH value of <3 With OR of 6.4 and CI of 95% of 0.901-45.5 respectively.

Conclusion: Laparoscopic ovarian procedure is a cost-effective procedure in comparison to multiple cycles of ovulation induction by CC and not for all ovarian disorders (endometriosis or premature ovarian insufficiency). The success rate of resolving infertility was high based on the ovulation and achieving pregnancy during the later phase reported as biochemical pregnancy or clinical pregnancy. Laparoscopy technique for ovarian drilling is considered a safe and effective treatment to resolve the anovulation in reproductive-age women.

Keywords: *Ovarian drilling, polycystic ovarian syndrome, clomiphene citrate.*

INTRODUCTION

Infertility is a critical and emotionally challenging issue for reproductive-age couples, affecting their physical and mental well-being. Globally, infertility impacts an estimated 15% of couples, with a higher prevalence reported in low-resource settings. The World Health Organization (WHO) has highlighted that approximately 25% of couples in developing countries are unable to conceive, attributing infertility to a combination of biological, environmental, and lifestyle factors [1]. In Pakistan, around 17% of couples experience infertility, and among these, 80% can eventually conceive with appropriate treatment. Male factors contribute to 40% of cases, female factors to 30%, and combined factors account for the remaining 30% [2, 3].

The global prevalence of polycystic ovary syndrome (PCOS) among women of reproductive age varies considerably depending on the diagnostic criteria applied. According to a systematic review and meta-analysis, the prevalence is estimated at approximately 6% using the National Institutes of Health (NIH) criteria, 10% with the Rotterdam criteria, and 10% with the Androgen Excess and PCOS Society (AES) criteria [4]. A more recent meta-analysis by Ding *et al.* (2023) further refined these estimates, reporting global prevalence rates of 5.5% (NIH), 11.5% (Rotterdam), and 7.1% (AES), with a pooled prevalence of 9.2% across all studies. These variations highlight the need for a standardized diagnostic approach to better understand the epidemiology and burden of PCOS worldwide [5, 6].

Polycystic ovarian syndrome (PCOS) is one of the leading causes of infertility in women, characterized by hormonal imbalances and metabolic dysfunction. PCOS affects 5–20% of women of reproductive age worldwide, leading to irregular menstrual cycles, anovulation, and a host of symptoms such as acne, hirsutism, obesity,

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and depression [4, 5]. The aetiology of PCOS is multifactorial, involving genetic, environmental, and endocrine disruptions, with insulin resistance playing a significant role in its pathogenesis [7].

Treatment strategies for PCOS-associated infertility often begin with lifestyle modifications and pharmacological interventions. Clomiphene citrate (CC), an anti-estrogenic drug, has been a first-line treatment for ovulation induction due to its efficacy and safety profile [8]. However, 20–25% of women with PCOS are resistant to CC and fail to ovulate, necessitating alternative therapeutic approaches [8]. In such cases, laparoscopic ovarian drilling (LOD) is often employed as a second-line treatment. LOD involves the creation of small perforations in the ovarian cortex using laser or diathermy to disrupt androgen-producing tissues, thereby restoring ovulation and hormonal balance [9].

Several studies have demonstrated the effectiveness of LOD in inducing ovulation and achieving pregnancy in CC-resistant women. Chundawat and Gupta reported that 66% of patients achieved regular menstruation, 60% ovulated spontaneously, and 48% conceived post-LOD [10]. Similarly, Hashim highlighted that LOD reduces ovarian androgen levels, normalizes the menstrual cycle, and enhances pregnancy rates [11]. However, the procedure is not without risks, including premature ovarian failure, adhesions, and tubal damage, which can further compromise fertility if not performed judiciously ovulation [9].

The precise mechanisms underlying LOD's efficacy remain under investigation, but current evidence suggests its role in modulating the hypothalamic-pituitary-ovarian axis. LOD is thought to lower intra-ovarian androgen levels and improve follicular responsiveness, thereby enhancing ovulatory function [10]. Despite these benefits, the procedure should be reserved for women who do not respond to less invasive treatments to minimize potential complications. Given the high prevalence of PCOS and the significant proportion of women resistant to CC, there is a pressing need to optimize therapeutic strategies. While LOD has demonstrated effectiveness in inducing ovulation and achieving pregnancy in clomiphene-resistant PCOS patients, concerns persist about its long-term impact on ovarian reserve and function. For instance, a meta-analysis observed a significant decline in serum anti-Müllerian hormone (AMH) levels post-LOD, suggesting potential alterations in ovarian reserve [12, 13].

Additionally, studies have reported variations in outcomes related to different surgical techniques, such as laser *versus* electrocautery, and the long-term sustainability of LOD's effects on menstrual regularity and fertility. These observations underscore the necessity for further research to optimize LOD protocols, assess their long-term safety, and establish comprehensive guidelines for their use in diverse PCOS populations [14].

Despite advancements in fertility treatments, infertility remains a significant challenge for women with polycystic ovary syndrome (PCOS), particularly those who are resistant to first-line treatments such as clomiphene citrate. Laparoscopic ovarian drilling (LOD) has emerged as a promising second-line therapy for these patients, yet there remains limited large-scale evidence assessing its long-term pregnancy outcomes and its potential to become a standard treatment option. Given the growing number of women with clomiphene-resistant PCOS seeking alternative treatment options, this study aims to fill this gap by reviewing pregnancy outcomes following LOD. Our findings will contribute to the current clinical discourse by evaluating the benefits of LOD as a second-line treatment, providing valuable insights for clinicians and patients alike.

MATERIALS AND METHODS

This retrospective chart review was conducted on secondary data to identify the effect of ovarian drilling on clients with PCOS who were resistant to Clomiphene Citrate and were unable to conceive before the drilling procedure. Data was retrieved from the case files of 133 couples available with the hospital's data bank for the past four years (Jan 2016 to 24 Dec 2019) by a non-probability consecutive sampling of women resistant to clomiphene citrate with PCOS. The place of study was the Australian Concept Infertility Medical Center, Clifton, Karachi.

Females were recruited based on inclusion and exclusion criteria, specifically focusing on both primary and secondary infertility. Participants were selected using non-probability consecutive sampling and met the following inclusion criteria: married women of reproductive age (less than 45 years), with patent fallopian tubes as confirmed by hysterosalpingogram and diagnosed with infertility based on hormonal assessments. Follicle-stimulating hormone (FSH) levels between 2 to 8 mIU/mL, luteinizing hormone (LH) levels between 1.34 to 30 IU/L, thyroid-stimulating hormone (TSH) levels between 0.4 to 2.5 mIU/L, and pprolactin range less than 25 ng/L were considered within the reference ranges for normal reproductive function [15-17]. Additionally, polycystic ovary syndrome (PCOS) was diagnosed based on the

Rotterdam criteria, which include the presence of at least two of the following three features: (1) irregular menstrual cycles (oligo-ovulation or anovulation), (2) clinical or biochemical hyperandrogenism, and (3) polycystic ovaries as observed on ultrasound [18]. Women with other conditions that could affect fertility, such as thyroid dysfunction or hyperprolactinemia, were excluded from the study.

Women with hyperandrogenism, diabetes mellitus, metabolic disorders, and other conditions such as uterine abnormalities, endometriosis, or male infertility factors (beyond sperm motility) were excluded from participation. Verbal consent was taken from the couple at the beginning of the telephone conversations, and recruited based on the eligibility criteria. Post-operative follow-up was conducted through regular outpatient visits, during which menstrual calendars were maintained and monitored. Patients were advised to record their menstrual cycles, and ovulation was verified through ultrasound and hormonal assays where necessary.

Independent variable was FSH, LH (day 2 of menstruation cycle): TSH, BMI, Prolactin, and Rapid Linear. The dependent variable was Pregnancy (biochemical or clinical), Pregnancy awaited, and Ovulation occurred. Outcome was defined as the achievement of one of the dependent variables: ongoing pregnancy, pregnancy awaited, or ovulation occurrence. It was determined through clinical confirmation of ovulation (*via* ultrasound and hormonal levels) or evidence of pregnancy based on beta-hCG levels and subsequent monitoring. Rapid linear represents semen with normal parameters and females with patent fallopian tubes. In our study, it was kept at >= 20 microns per second. The participants were categorized based on BMI: normal or healthy weight (BMI 18.5–24.9), overweight (BMI 25–29.9), obese (BMI ≥30), and underweight (BMI <18.5).

The descriptive variables were analyzed using frequency tables and the inferential statistics were analyzed using Statistical Package for Social Sciences (SPSS software version 21). To analyze the association between the categorical variables, Fisher's exact test and Chi-square test were employed to assess statistical significance across the different groups

The approval was obtained from the SZABIST Ethical Committee with Reference. No IERB(5)/SZABIST-KHI(MSPH)/18104111/190109. The permission was also taken from the private infertility clinic. Confidentiality was observed in the collection of the data. Confidentiality was observed, as all data was stored in the safe room of the fertility clinic and only relevant data was accessed by the primary investigator. There was no anticipated harm to the participants as we are dealing with secondary data. A verbal consent was obtained during the telephone conversation with the couples.

RESULTS

A total of 133 patients were enrolled in the study; the mean age of 28.94±4.97 years was categorized into two groups 20-29 years with 74 (55.6%) patients while 30–39-year category had 59 (44.4%) patients respectively. Body Mass Index (BMI) was reported as < 18.5 (underweight) in 5 (3.8%), 18.5-24.9 (normal) in 55 (41.4%), 25-29.9 (Overweight) in 61 (45.9%) and > 30 (Obese) in 12 (9%) patients respectively (**Table 1**).

Ninety-three (69.6%) patients reported primary infertility while 40 (30.1%) were diagnosed with secondary infertility, 96 (72.2%) were diagnosed for less

Table 1: Demographic information.

Variables	Categories	Frequency	Percentage
Age	20 – 29 years	74	55.6
	30 – 39 years	59	44.4
Ethnicity	Sindhi	52	39
	Urdu speaking	61	46
	Punjabi	12	9
	Saraiki	2	2
	Baluchi	3	2
	Pathan	3	2
Religion	Muslim	101	76
	Hindu	27	20
	Christian	5	4
BMI*	Less than 18.5 (Underweight)	5	3.8
	18.5 – 24.9 (Normal or Healthy weight)	55	41.4
	25 – 29.9 (Overweight)	61	45.9
	30 and more (Obese)	12	9.0

**BMI: Body Mass Index.*

Table 2: infertility type and duration in study population.

Variables	Categories	Frequency	Percentage
Infertility type	Primary	93	69.9
	Secondary	40	30.1
Infertility duration	Less than five years	96	72.2
	Five – ten years	37	27.8
R-Linear*	< 29	96	72.2
	30 – >40	37	27.8
Patency	LP*	13	9.8
	BLP*	120	90.2

**R-Linear: Rapid Linear, LP: Left patent fallopian tube, BLP: Bilateral patent fallopian tube.*

than 5 years and 37 (27.8%) had infertility diagnosis for more than 5 years. After the flow of the menstrual cycle categorized as Right and left were reported in categories with 10-20 and 21-30, indicating 128 (96.2%) and 5 (3.8%) respectively on the Right side and 106 (79.7%) and 27 (20.3%) respectively on the left side (**Table 2**).

Follicular stimulating hormones (FSH) and luteinizing hormones (LH) were reported as ≤05-07 and 8-≥10 with 106 (79.7%), 27 (20.3%) and 113 (85%) and 20 (15%) for FSH and LH respectively. Prolactin was categorized as <5-15 and 16-30 with 67 (50.4%) and 66 (49.6%) respectively. TSH was reported as <3 In 112 (84.2%) and 3-6 in 21 (15.8%), Patency was reported as LP and BLP with frequency of 13 99.8%) and 120 (90.2%) while R Linear was reported as <29 and 30-40 and frequency was 96 (72.2%) and 37 (27.8%) respectively (**Table 3**).

Evidence based ovulation was seen by tracking follicles through ultrasound and hormones showing ovulation has occured in 90-95% of females (**Fig. 1**).

Table 3: Menstrual cycle flow and hormonal level.

Variables	Categories	Frequency	Percentage
After flow RT	10 - 20	128	96.2
	21 – 30	5	3.8
After flow LT	10 - 20	127	95.5
	21 – 30	6	4.5
FSH	< 5 - 7	106	79.7
	8 – >10	27	20.3
LH	< 5 - 7	113	85.0
	8 – >10	20	15.0
Prolactin	< 5 - 15	67	50.4
	16->30	66	49.6
TSH	< 3	112	84.2
	3->6	21	15.8

RT: Right Tube; LT: Left Tube, FSH: Follicle Stimulating Hormone; LH: Luteinizing hormone; TSH: Thyroid Stimulating Hormone.

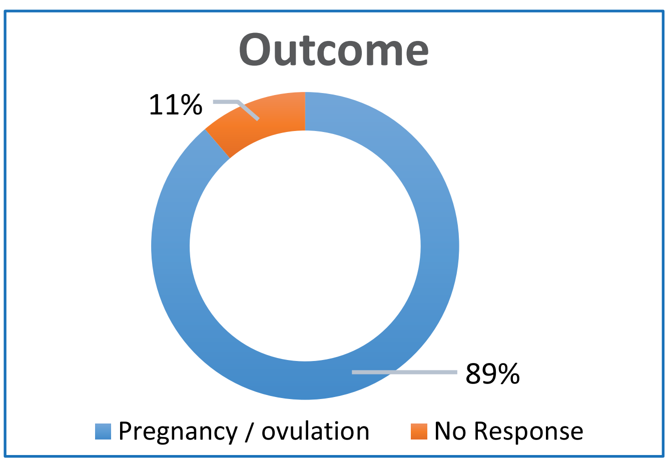

Fig. (1): Frequency of pregnancy outcome.

Table 4: Pregnancy and ovulation outcomes following laparoscopic ovarian drilling.

Variables	Frequency	Percentage
Pregnancy ongoing	67	50.4
Pregnancy awaited	19	14.3
Ovulation occurred	41	30.8
Cycle disturbed	6	4.5
Total	133	100

Table 5: Association of hormonal level with pregnancy outcome.

Variables	Categories	Significance	OR	95% CI
FSH	< 5 - 7	0.002	18.8	2.97-119.9
LH	< 5 - 7	0.32	0.395	0.063-2.46
Prolactin	< 5 - 15	0.159	0.285	0.050-1.63
TSH	< 3	0.063	6.4	0.901-45.5

FSH: Follicle Stimulating Hormone; LH: Luteinizing hormone; TSH: Thyroid Stimulating Hormone; OR: Odds Ratio; CI: Confidence Interval.

Out of 133 participants, 50.4% had ongoing pregnancies, 14.3% were awaiting pregnancy, and 30.8% showed evidence of ovulation. Only 4.5% experienced cycle disturbances following the intervention (**Table 4**).

The outcome of the study was associated with determinants including FSH levels, LH levels, Prolactin levels and TSH levels respectively. The Odds of negative response to ovarian drilling were reported with FSH value of <5-7 with OR of 18.8 and CI 95% of 2.97-119.9, LH value of <5-7 with OR of 0.395, CI 95% of 0.063-2.46, Prolactin of <5-15 with OR of 0.285 and CI 95% of 0.050-1.63 while TSH value of <3 With OR of 6.4 and CI of 95% of 0.901-45.5 respectively (**Table 5**).

DISCUSSION

Our study found that approximately 95% of women undergoing laparoscopic ovarian drilling (LOD) either became pregnant, were in the process of becoming pregnant, or began ovulating, indicating a high potential for future pregnancy. This aligns with previous research demonstrating the effectiveness of LOD in inducing ovulation and achieving pregnancy in women with polycystic ovary syndrome (PCOS). For instance, a study reported an ovulation rate of 92% and a pregnancy rate of 80% following LOD in clomiphene-resistant PCOS patients. Similarly, a study observed a cumulative ovulation rate of 73% and a pregnancy rate of 37% within two years post-LOD. These findings support the role of LOD as an effective treatment modality for inducing ovulation and enhancing fertility outcomes in women with PCOS [19].

The results of our research back with the conclusions drawn by another study that there is a substantial connection between the duration of infertility, body mass index, and the FSH/LH ratio and the pregnancy outcome [20]. The results of this study, together with other studies [21] indicate that LOD is an effective alternative treatment option for the management of PCOS. Similar to our findings of successful ovulation and pregnancy outcome another study evaluated the effectiveness of LOD and letrozole to induce ovulation among patients with clomiphene-resistant PCOS [22].

The extracted data was analyzed, and the researchers concluded that there was no significant difference between the two treatment options in terms of inducing ovulation and achieving live births. Both Seow *et al.* [23] and our study reached similar outcomes, indicating that pregnancy and overall ovulation rates can be as high as 90% with our data showing a slightly higher rate of 95% [9]. On the other hand, Seow *et al.* are of the notion that LOD could produce a drop in LH and insulin. They warned that postoperative adhesion is a frequent example of a negative consequence caused by LOD.

It has been hypothesized that LOD functions by reducing androgen production within the ovaries [24]. One of its advantages is that it typically eliminates the risk of multiple pregnancies. Additionally, LOD is considered more cost-effective and has a better safety profile compared to other treatments [25]. Studies have shown a decrease in both LH and androgen levels following LOD, supporting its effectiveness as a treatment for women with PCOS who are resistant to clomiphene citrate [12].

LIMITATIONS

The research however faced limitations as well due to the nature of the study constituted the issues surrounding infertility and external factors faced during the collection of secondary data. The study had a restricted sample size and lack of a control group, attributed to logistical and operational challenges as a vast sample size at the facility for laparoscopic ovarian procedures was not available.

Only patients recruited for the study up to one year after the LOD procedure were included, with most pregnancies occurring within 6-12 months postoperatively. However, there were limitations in measuring the exact time frame for achieving pregnancy, as the data were retrieved retrospectively after pregnancy had already occurred. As the study was retrospective in nature and data were extracted from medical records, participants were not followed up for specific timelines regarding ovulation and pregnancy outcomes. Therefore, postoperative follow-up details, such as the duration of monitoring for ovulation and pregnancy success, were not available. This limitation should be considered when interpreting the results, as the absence of detailed follow-up data restricts a more precise understanding of the long-term effectiveness of LOD for fertility outcomes.

However, due to cultural associations, taboos, and myths, a major problem was getting approval from the relevant authorities as they were reluctant to share data regarding infecundity. Regionally, diets, climate and lifestyle could not be accounted for due to the limitation in time and resources required to conduct the study.

CONCLUSION

The laparoscopic ovarian procedure is cost-effective in comparison to multiple cycles of ovulation induction by CC, Gonadotropins and Assisted reproductive technique (ART) which can only be afforded by the affluent class. The success rate of resolving infertility was high based on ovulation and achieving pregnancy during the later phase reported as biochemical pregnancy or clinical pregnancy. LOD is primarily used for CC-resistant PCOS and not for all ovarian disorders (endometriosis or premature ovarian insufficiency). Laparoscopy technique for ovarian drilling is considered a safe and effective treatment to resolve the anovulation in reproductive-age women.

LIST OF ABBREVIATIONS

LOD : Laparoscopy Ovarian Drilling
CC : Clomiphene Citrate
BMI : Body Mass Index
FSH : Follicle Stimulating Hormone
HSG : Hysterosalpingogram
IVF : *In Vitro* Fertilization
LH : Luteinizing Hormone
PCOS : Poly Cystic Ovary Syndrome
TSH : Thyroid Stimulating Hormone
LP : Left Patent Fallopian Tube
BLP : Bilateral Patent Fallopian Tube

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Ethical Review Board of Shaheed Zulfiqar Ali Bhutto Institute of Science and Technology (SZABIST), Karachi (REF letter No. IERB(5)/SZABIST-KHI(MSPH)/18104111/190109). All procedures performed in studies involving human participants were by the ethical standards of the institutional and/ or national research committee and the Helsinki Declaration.

CONSENT FOR PUBLICATION

Informed consent was taken from patients, whose medical records were reviewed.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORS' CONTRIBUTION

RJ guarantor of the integrity of the entire study. RJ and NS generate study concepts and design. NJ did literature research, and ST collected data. RJ and NS analyze the data. HS and UI prepared a manuscript. The manuscript was critically reviewed and revised by RJ. All authors have read and approved the manuscript.

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