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Original Article

Role of laparoscopic ovarian drilling in treatment of infertility among PCOS patients in a tertiary care hospital

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ABSTRACT

Introduction: *Anovulatory infertility is present in 75% of patients with polycystic ovarian syndrome (PCOS), in addition to oligomenorrhoea and signs and symptoms of hyperandrogenism. In patients with PCOS, resolution of infertility is an important goal of treatment. Laparoscopic ovarian drilling (LOD) is an alternative to ovulation induction with gonadotrophins for PCOS patients unresponsive to clomiphene citrate.* ***Aim of the study:*** *The aim of the study was to observe the successful ovulation outcome of patients after laparoscopic ovarian drilling* ***Methods:*** *This Quasi-experimental study was conducted at the Department of Obstetrics and Gynaecology, BIRDEM General Hospital, Dhaka, Bangladesh. The study duration was 1 year, from January 1st to December 31st of 2011. Using a non-probability convenient sampling method, a total of 45 patients were selected from the outpatient department of Obstetrics and Gynaecology in BIRDEM hospital following the exclusion and inclusion criteria.* ***Result:*** *Among 45 PCOS patients 40 (88.9%) started to menstruate regularly after LOD and the improvement was significant as compared to 17.8% before LOD (p <0.000). An overall pregnancy rate of 15.6% was achieved following LOD within 6 months (p <0.006). However, age, duration of infertility, BMI did not emerge as significant factors to have an impact on successful reproductive outcomes.* ***Conclusion:*** *Women with polycystic ovarian syndrome respond favorably to laparoscopic ovarian drilling. LOD may avoid or reduce the need for gonadotrophins for ovulation induction.*

Keywords: *Ovaries, Infertility, Laparoscopic Ovarian Drilling, Polycystic Ovarian Syndrome (PCOS)*

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INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) is a common endocrine disorder in women of reproductive age and the most common cause of anovulatory infertility which accounts for more than 70% of all cases[1].It is thought to occur in 5-10% of women of reproductive age globally[2]. The pathology of PCOS was described by Stein and Leventhal in 1935 as a heterogeneous disorder of unknown etiology characterized by hyperinsulinemia with insulin resistance, hyperandrogenemia, and high luteinizing hormone level[3],[4]. Manifestations like menstrual irregularity, hirsutism, and chronic anovulation are related to the hyperandrogenic state in these women[5]. The most common presenting feature of PCOS is anovulatory infertility, which accounts for 45% of all presenting symptoms. A proposed mechanism for anovulation and elevated androgen level suggests that, under the increased stimulatory effect of LH secreted by the anterior pituitary, stimulation of the ovarian theca cell is increased. In turn, these cells increase the production of androgen (testosterone and androstenedione). Because of a decreased level of follicle-stimulating hormone (FSH) relative to LH, the ovarian granulosa cells cannot aromatize the androgen to estrogen, which leads to decreased estrogen level and consequent anovulation. Anovulatory infertility is a prevalent issue in PCOS women. Since the etiology of PCOS is uncertain, the treatment has mainly been directed towards symptomatic control. There are many modalities of treatment for PCOS-related anovulatory infertility. The first line of treatment is to induce ovulation is clomiphene citrate (CC)[6]. CC has a successful ovulation rate of almost 80%[7],[8]. Studies of clomiphene-resistant patients treated with either metformin, an insulin sensitizer, or letrozole, an aromatase inhibitor yielded mixed results[9]. Patients who remain anovulatory after oral agent therapy are usually treated with gonadotrophins. Ovulation induction with gonadotrophins is well established in patients resistant to CC, but extensive monitoring is necessary due to the high sensitivity of PCOS to exogenous gonadotrophins. The risk of multiple follicle development leading to termination of the cycle, possible ovarian hyperstimulation syndrome (OHSS), and multiple pregnancies can be as high as 20%, with miscarriage rates being even higher[10]-[12]. In addition, gonadotrophin therapy is costly as well as time-consuming. Ovarian drilling is an alternative approach in treating CC-resistant patients with PCOS. Laparoscopic Ovarian Drilling (LOD) is a procedure involving the breaking of the thick outer surface of the ovaries, increasing the testosterone levels produced by the ovaries. It is a simple procedure with minimal morbidity and can lead to consecutive ovulation with minimal risks of multiple pregnancies [13]. Sensitivity to CC is also increased after LOD [14]. After successful LOD, many studies have reported high ovulation and pregnancy rates [15],[16]. To date, several combined or alternative treatments have been proposed for inducing ovulation in clomiphene citrate-resistant PCOS patients. Till now the data published regarding traditional second steps for inducing ovulation in PCOS patients are not completely satisfactory. Medical treatment with gonadotrophin needs intensive monitoring. As an alternative to gonadotrophin therapy, laparoscopic ovarian drilling (LOD) was most recently proposed to maximize ovulation and pregnancy benefits. There is evidence that LOD may enhance endocrine status as well as reproductive results in PCOS patients. On the basis of this consideration, the present study was

designed to assess the effectiveness of laparoscopic ovarian drilling (LOD) in the treatment of infertility in PCOS patients via their outcome.

OBJECTIVE

GENERAL OBJECTIVE

- To assess the effectiveness of laparoscopic ovarian drilling in the treatment of infertility of PCOS patients

SPECIFIC OBJECTIVES

- To ascertain the changes in menstrual pattern and pregnancy rate

METHODS

This Quasi-experimental study was conducted at the Department of Obstetrics and Gynaecology, BIRDEM General Hospital, Dhaka, Bangladesh. The study duration was 1 year, from January 1st to December 31st of 2011. Using a non-probability convenient sampling method, a total of 47 PCOS patients with infertility were selected from the inpatient department of Obstetrics and Gynaecology in BIRDEM hospital following the exclusion and inclusion criteria who had undergone laparoscopic ovarian drilling. During follow-up, two subjects were lost, leaving the final sample size of 45. Infertility was categorized as being unable to conceive for over 12 months at a minimum. Informed written consent was obtained from all the participants, and ethical approval was obtained from the ethical review committee of the study hospital. Following ovarian drilling, the women were asked to keep a record of their menstrual cycle and to take ovulation-inducing drugs (clomiphene citrate 100 mg orally at night or letrozole 2.5 mg twice daily orally) from D2—D6 of the menstrual cycle for 4 to 6 cycles. The patients were followed up to 6 months following LOD in the outpatient department. Any change in the menstrual pattern and pregnancy rate was documented. All statistical tests were two-sided and a significance level of 0.05 was followed. All the data analysis and statistics were performed using the SPSS 16.0.

Inclusion Criteria

- Married women of the age group of 20 - 40 years
- Documented PCOS (clinically, USG or laboratory) who underwent laparoscopic ovarian drilling
- Treated with ovulation-inducing drugs (clomiphene citrate, aromatase inhibitor, inj. gonadotrophin) previously, but failed to get pregnant
- BMI between 20-35kg/m2
- Patients who had given consent to participate in the study.

Exclusion Criteria

- Severe male factor infertility
- Hypothyroidism
- Severe endometriosis
- Hyperprolactinemia
- Premature ovarian failure
- Bilateral tubal block

RESULT

Table 1: Demographic characteristics of PCOS patients (n=45)

Characteristics	Mean ± SD	Range
Age (years)	28.51 ± 4.67	20-38

Duration of infertility (years)	6.26 ± 3.92	1-16
BMI (kg/m2)	26.75 ± 4.28	22.47-31.03
Waist to hip ratio	0.92 ± 0.07	0.85-0.99
Socioeconomic status	**Frequency**	**Percentage**
Upper Middle	2	4.4
Middle	20	44.4
Lower	23	51.1
Infertility		
Primary	33	73.3
Secondary	12	26.7
Obese		
Yes	9	20
No	36	80
History of DM		
Yes	6	13.3
No	39	86.7

In the present study, the age of the patients ranged from 20-38 years with a mean of 28.51 years. The duration of infertility among the participants ranged from 1-16 years with a mean of 6.26 ±3.92 years. BMI and Waist to Hip ratio were 26.75 ± 4.28 and 0.92 ± 0.07 respectively. Most of the participants belonged to the lower and middle classes, while only 4.4% were from the upper-middle class. 73.3% of the participants faced primary infertility, while 26.7% faced secondary infertility. Only 20% of the participants were obese, and 13.3% had a history of diabetes (DM)

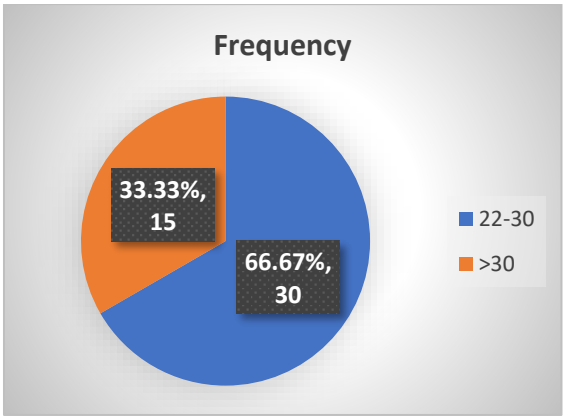

Figure 1: Age distribution of the participants in years (n=45)

Among the participants, the majority (66.67%) were older than 30 years of age, while the remaining 33.33% were from the age group of 22-30 years. The Mean ± SD age of the participants was 28.51 ± 4.67 years.

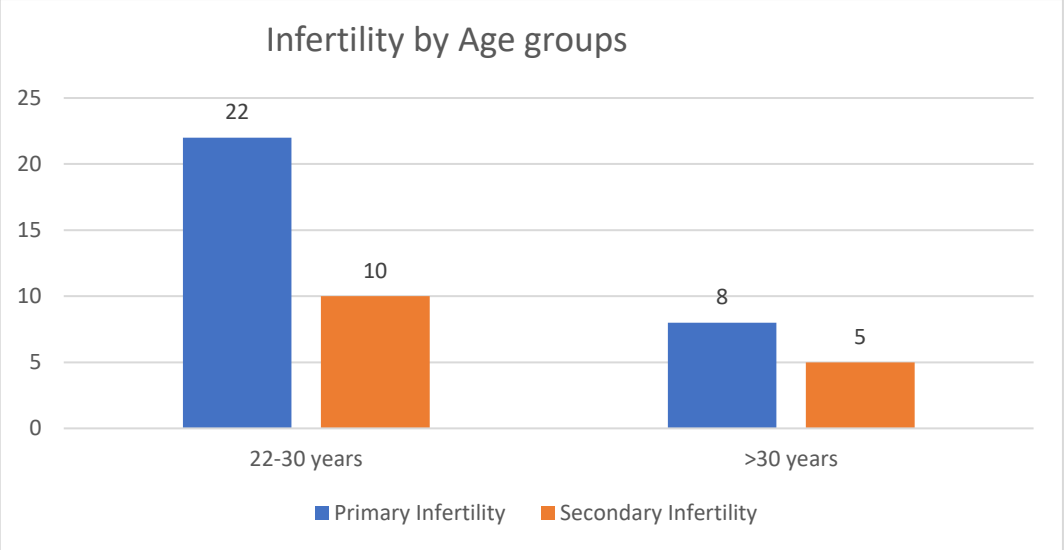

Figure 2: Distribution of participants with infertility by age groups (n=45)

22 (48.9%) of patients with primary infertility were in the age group of 20-30 years whereas 10 (17.8%) were above 30 years of age. In the case of secondary infertility, 8 (22.2%) of the patients were within 20-30 years. And the remaining 5 (11.1%) were above 30 years of age. There was no significant difference between age groups in infertility patients

Table 2: Clinical characteristics of PCOS patients (n=45)

Characteristics	Frequency	Percent
Hirsutism	36	80.00%
Acne	25	55.56%
Oligomenorrheic	33	73.33%
Amenorrhoeic	2	4.44%
Menorrhagic	1	2.22%

Clinical features of hyperandrogenism i.e., hirsutism and acne were present in 36(80%) and 25 (55.5%) respectively. An irregular menstrual cycle pattern was observed in 37 (82.2%) of the participants, among whom, 33 (73.33%) were oligomenorrheic, 2 (4.44%) were amenorrhoeic, and the remaining 1 patient was menorrhagic.

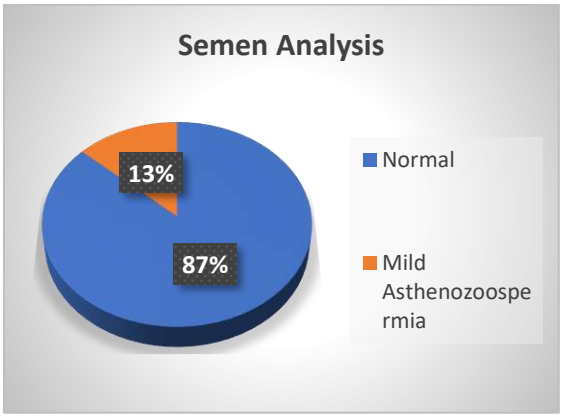

Figure 3: Semen analysis of the male counterparts of patients (n=45)

As severe male factor infertility was an exclusion criterion of the present study, semen analysis was normal for the majority (87%) of the participants, while 13% had mild asthenozoospermia.

Table 3: Laparoscopic Findings of PCOS patients (n=45)

Laparoscopic findings	Frequency	Percentage
Uterine Size		
Normal	33	76.7
Smaller	3	7.0
Bulky	7	16.3
Uterine Shape		
Regular	43	95.6
Irregular	2	4.4
Right ovary		
Normal	2	4.5
Slightly enlarged and polycystic	7	15.5
Moderately enlarged and polycystic	36	80.0
Left ovary		
Normal	2	4.5
Slightly enlarged and polycystic	9	20.0
Moderately enlarged and polycystic	34	75.5
Adhesion		
Yes	4	8.9
No	41	91.1

Most of the ovaries were found to be bilaterally enlarged and polycystic except a few who had unilateral enlargement 4 (8.9%). Mild adhesion was present in 4 (8.9%) of patients. 36 (80%) of the participants had moderately enlarged and polycystic right ovary, and 7 (15.5%) had slightly enlarged and polycystic right ovary. 75.5% of the participants had moderately enlarged and polycystic left ovary, and 9 (20%) had slightly enlarged and polycystic left ovary.

Table 4: Menstrual pattern of PCOS patients at baseline and 6-month follow-up after Laparoscopic Ovarian Drilling (n=45)

Menstrual pattern	**Baseline**				**Six months later**				**P-value**
	Regular		**Irregular**		**Regular**		**Irregular**		
	N	(%)	N	(%)	N	(%)	N	(%)	<0.001
	8	17.8	37	82.2	40	88.9	5	11.1	

At the start of the study, the menstrual pattern was irregular in 37(82.2%) and regular in 8 (17.8%) of PCOS patients. At the follow-up six months after LOD, 40

(88.9%) of patients resumed regular menstruation whereas 5 (11.1%) failed to do so. The improvement of the menstrual pattern of PCOS patients after LOD was highly significant, (p<0.001) as compared to baseline.

Table 5: Pregnancy rate of PCOS patients at baseline and 6-month follow-up after Laparoscopic Ovarian Drilling (n=45)

Pregnancy rate	Baseline				Six month later				P-value
	Positive		Negative		Positive		Negative		
	N	(%)	N	(%)	N	(%)	N	(%)	0.006
	0	0.0	45	100.0	7	15.6	39	84.4	

Total pregnancies achieved after LOD with ovulation-inducing drugs were 7 (15.6%). The pregnancy rate of PCOS patients after LOD was statistically significant as compared to before treatment (p <0.05).

DISCUSSION

Polycystic ovarian syndrome (PCOS) is a relatively common condition in women during their reproductive age. It is characterized by chronic anovulation, androgen excess, hypersecretion of luteinizing hormone (LH), obesity, and infertility. Despite medical advances, this syndrome has low understandability and has a varying degree of severity and symptomologies. As the presenting symptoms of these groups of patients are quite often infertility due to chronic anovulation, restoration of anovulatory function assumes paramount importance. Oral clomiphene citrate is the usual treatment for anovulatory women with PCOS. For all PCOS patients who have a poor reaction to clomiphene citrate, the therapy options include medical ovulation induction with greater dosages, use of aromatase inhibitor, or stronger stimulants such as gonadotrophin, or laparoscopic surgery. Because of the high percentage of ovulation and conception that occurs following its implementation, laparoscopic management of PCOS anovulatory infertility has become a frequent method for the treatment of clomiphene citrate-resistant patients. Also, postoperative adhesions are lower compared to bilateral wedge resection by laparotomy. Such a surgical method also eliminates the risk of ovarian hyperstimulation syndrome (OHSS). Additionally, high cost and intensive monitoring associated with gonadotrophin can be avoided. In this study, we have analyzed the impact of laparoscopic ovarian drilling (LOD) on menstrual cycle regularity and pregnancy rate after 6 months of follow-up. 45 women with a mean age of 28.51 ± 4.67 years and mean infertility duration of 6.26 ± 3.92 years, BMI of 26.75 ± 4.28 kg/ m2 entered into the study. Hirsutism and acne were reported in 80% and 55.5% of PCOS patients respectively. All of our subjects had been unsuccessfully treated with clomiphene citrate (CC) or letrozole or gonadotrophin or metformin plus CC/ letrozole. Patients underwent LOD and were advised to take clomiphene citrate or letrozole depending upon individual assessment. Restoration of the menstrual cycle was measured at 6 months after LOD. In our study proportion of PCOS patients who resumed regular menstrual patterns after LOD rose from 17.8% to 88.9%. The incidence is statistically significant. In the study group, 17.8% of women had regular menstrual cycles prior to LOD.

Although chronic anovulation in women with PCOS is usually associated with menstrual irregularities (38), several studies have reported that a proportion of these women do have apparently 'regular' menstrual cycles. One study reported that 21% of anovulatory PCOS women have regular menstrual cycles [17]. Another study reported a 24% incidence of regular menstrual cycles among anovulatory PCOS patients undergoing ovarian diathermy[18]. In a study of 1741 women with PCOS, 30% of patients had regular cycles [19]. In the present study, the proportion of women with regular menstrual cycles increased significantly from 17.8% before LOD to 88.9% (p-value < 0.000) after the laparoscopic procedure. Similar findings were reported in many other studies, with restored menstrual regularity in a significant proportion [16],[20],[21]. Concerning reproductive outcomes, in the present study, a total of 7 (15.6%) patients achieved pregnancy within 6 months after laparoscopic surgical procedure (LOD). 3 (6.7%) women conceived with clomiphene citrate as a supplementary treatment after LOD, 4 (8.9%) conceived with the aid of letrozole. Among these pregnancies, one was a twin pregnancy and one ended in miscarriage. Widely variable rates of pregnancy have been reported following LOD in different studies, with most estimates between 50% and 80% within 1 year of the procedure [22]. One study reported that a total of 56 patients achieved pregnancy in the whole cohort (cumulative pregnancy rate 63%) and 31 (35%) achieved pregnancy within 12 months. For those who conceived spontaneously (n=31), the median duration to get pregnant was 11 (3-26) months after LOD [23]. The variability in pregnancy rates following LOD may be due to heterogeneous samples and the results of some studies may not be stratified for age or difference of LOD technique, and they may fail to exclude patients with other infertility factors [24] .

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

Laparoscopic ovarian drilling is a cost-effective, safe, and minimally invasive treatment for PCOS patients with anovulatory infertility. A single procedure results in uni-follicular ovulation and conception. No need for continuous monitoring as seen with gonadotrophin treatment. No fear of multiple births and ovarian hyperstimulation syndrome. The low parity pregnancy rate may also be attributed to the nature of patients included in this study who are resistant anovulatory patients and had multiple courses of different ovulation induction. A short follow-up period (only 6 months) was another important factor and a longer follow-up may add a new number of pregnancies.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

RECOMMENDATION

Further study with a large sample size in different tertiary care centers is suggested. In addition, post-LOD detailed hormone study and long-term follow-up are recommended.

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