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**Original Research Article**

# Fertility benefits of controlled ovarian stimulation and intrauterine insemination in different stages of endometriosis in a fertility centre in Southern India: a retrospective study

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## ABSTRACT

**Background:** To determine the fertility benefit of controlled ovarian hyperstimulation and intra uterine insemination (IUI) in different stages of Endometriosis. It was a retrospective observational study done in Kinder women's hospital and fertility centre, Cherthala, Kerala, India.
**Methods:** A retrospective analysis of 100 patients with isolated endometriosis (I and II vs. III and IV) who underwent IUI between January 2018 to December 2019 were selected. Cycle fecundity rates and clinical pregnancy rates and pregnancies above 28 weeks were measured. Clinical pregnancy rates with COH and IUI were also compared between grade I/II vs III/IV endometriosis.
**Results:** A total of 16 (16%) pregnancy were achieved with controlled ovarian hyperstimulation (COH) and IUI in patients with endometriosis which included 11 (11%) clinical pregnancies and 5 (5%) miscarriages. 10% clinical pregnancies were achieved in grade I/II endometriosis and 1% in grade III/IV endometriosis. 68.75% of the pregnant patients progressed to pregnancy of >28 weeks.
**Conclusions:** The grade of endometriosis affected the clinical pregnancy rate in COH with IUI. The treatment success of COH with IUI was noted to be greater in minimum or mild endometriosis i.e., grade I/II. The treatment modality is ineffective in moderate to severe grades of endometriosis i.e., III/IV.

**Keywords:** Intrauterine insemination, Endometriosis, Infertility, IVF

## INTRODUCTION

Endometriosis is defined as the presence of endometrial like tissue outside the uterus, which induces chronic inflammatory reaction.[1] The prevalence of endometriosis is estimated to range from 2-10% in general female population and up to 50% in infertile population.[2] While some women may not have any symptoms many experiences severe pain and or infertility.

Since many years the correlation between endometriosis and infertility has been debated. The fecundity ranges between 0.15 to 0.20/month in normal couple, while it tends to be very low of about 0.02-0.1/month in endometriosis.[3,4] The treatment plan depends on the grade of endometriosis. Many treatment options have been proposed to treat couples with endometriosis and infertility. These options range from no treatment to controlled ovarian hyperstimulation (COH) and IUI or *in vitro* fertilization (IVF) and embryo transfer (ET).

According to European Society of Human Reproduction and Endocrinology (ESHRE) and American society for reproductive medicine (ASRM) IUI is only recommended in sub fertile women with minimal to mild (I/II) endometriosis.[1] There is little documented evidence with

conflicting results on the effect of COH and IUI after laparoscopy on the pregnancy outcome. The aim of the present study is to assess if COH with IUI has a significant effect on clinical pregnancy rates (CPR) and live birth rates (LBR) in different grades of endometriosis after laparoscopic surgery.

## METHODS

This study retrospectively analysed patients with surgically confirmed endometriosis (ASRM grading) who underwent COH with IUI at Kinder Women's Hospital and Fertility Centre, Kerala from January 2018 to December 2019. Various stages of endometriosis was identified by direct visualization in accordance with revised ASRM classification in the 100 patients included in the study. They were divided into two groups (I/II) and (III/IV) depending on the laparoscopic findings. Electrocoagulation of the peritoneal implants, adhesiolysis and removal of ovarian endometrioma were done in indicated cases. Demographic data, duration and type of subfertility were recorded. The patients were treated with letrozole 5 mg/day from day 3 to day 7 of menstrual cycle and 75 IU of IM HMG on day 3 and day 9 of the cycle. If the dominant follicle did not reach the required size, an additional dose of 75 IU HMG was given. When the dominant follicle was ≥17 mm, 5000 IU HCG (human chorionic gonadotropin) was given. Standard protocols were used for insemination. The semen sample was obtained by masturbation. Semen was washed by swim up technique. IUI was performed 36 hours after HCG administration. All IUI were performed by the same 2 authors. Luteal phase was supported with progesterone. Urine pregnancy test (UPT) was done on day 16 after IUI. A serum HCG was done if UPT was positive. Clinical pregnancy was confirmed after 2 weeks of positive UPT by trans vaginal sonography by the presence of intrauterine gestational sac and cardiac activity. All patients who achieved clinical pregnancy were followed up till their delivery.

### *Statistical analysis*

Statistical analysis was performed using SPSS version 23.0 (IBM SPSS, USA). Data were expressed as mean ± standard deviation (SD) OR N (%). Non parametric data were expressed as medians with range. Differences between the two groups were evaluated using the Student's t-test (continuous data) or Mann-Whitney U-test in case of non-parametric data and chi-squared or Fisher's exact tests for categorical data. A $p<0.05$ was considered significant.

## RESULTS

A total of 100 patients (Table 1) with different grades of endometriosis underwent IUI at Kinder Women's Hospital between January 2018 to December 2019. Among these 100 patients, 84 patients had primary subfertility while 16 were secondary sub fertile (Figure 1).

**Table 1: Outcomes of intrauterine insemination in Grade I/II Vs III/IV endometriosis.**

| Parameters | Grade I/II | Grade III/IV | P value (Mann-Whitney test) |
|---|---|---|---|
| **Primary subfertility** | 67 | 17 | - |
| **Secondary subfertility** | 12 | 4 | - |
| **UPT+** | 13 | 3 | -0.240, 0.810 |
| **Clinical Pregnancy** | 10 | 1 | -1.023, 0.306 |
| **Pregnancy lasting for more than 12 weeks** | 10 | 1 | -1.023, 0.306 |
| **Miscarriage** | 3 | 2 | -1.065, 0.287 |

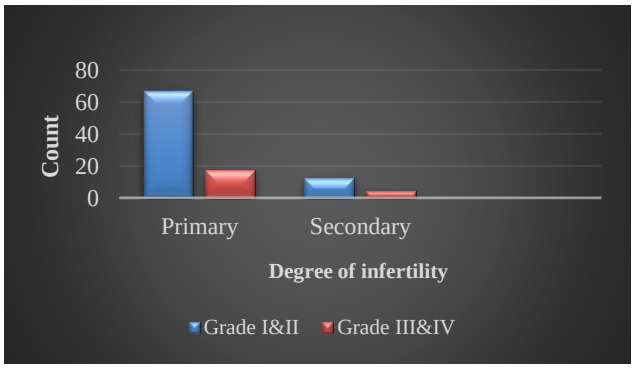


**Figure 1: Primary and secondary infertile patients in grade I/II verses III/IV endometriosis.**

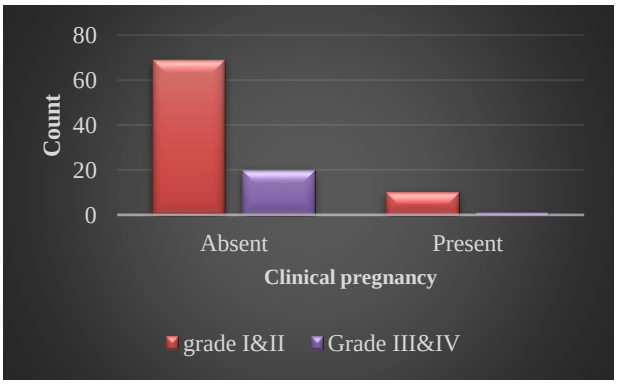


**Figure 2: Clinical pregnancy following IUI in grade I/II verses III/IV endometriosis.**

A total of 289 IUI cycles were performed (Table 2). 16 patients had a positive urine pregnancy test which included 13 grade I and grade II endometriosis and only 3 in grade III and grade IV endometriosis. The clinical pregnancy rate was 11% in the entire study group which included 10% in grade I and grade II endometriosis group

and just 1% in grade III and grade IV endometriosis (Figure 2). 5 pregnancies ended up in miscarriage.

**Table 2: Number of cycles of intrauterine insemination in grade I/II Vs III/IV endometriosis.**

| Parameters | | Grade I/II | Grade III/ IV |
|---|---|---|---|
| **Number of cycles of IUI** | 1 | 1 | 2 |
| | 2 | 1 | 4 |
| | 3 | 19 | 73 |

## DISCUSSION

The pathogenesis of endometriotic lesions is not fully understood. Medical management for endometriosis is often used for symptomatic disease or as an adjunct to surgical management of pelvic pain or infertility. One of the significant findings in our study is the probability of conception is significantly higher after integrated laparoscopy with COH+IUI especially in those with a milder form of the disease. Superovulation could correct the minimal pre-ovulatory endometrial defects[5] and the subtle ovulatory disorders found in some women with endometriosis.[6]

More than about two third women with endometriosis in our study did not benefit from three cycles of COH+IUI after laparoscopy. This could be due to the immunological or biochemical factors associated with endometriosis. Vollenhoven et al studied the effectiveness of HMG with IUI for treatment of infertility.[7] The cycle fecundity rate was 7% for male factor, 11% for oligoovulation, 8% for tubal/pelvic factor, 13% for minimal endometriosis, 18% for mild endometriosis and 17% for moderate endometriosis. Geber et al showed in their study that despite a little decrease of pregnancy rate in minimal and mild endometriosis subgroup, there was no significant difference in pregnancy rate between minimal and mild to moderate and severe endometriosis groups. In our study the pregnancy rate in stage I/II was significantly higher although adhesiolysis was performed during laparoscopic procedure in moderate to severe cases.[8]

In a study done by Kereszturi et al CPR in stage I/II was 64.6% following COH with IUI and in stage III/IV was 45.6%.[9] However, our study showed a CPR of 10% in stage I/II and 1% in stage III/IV. Based on our results COH with UI could therefore be offered to patients as a treatment option after laparoscopy in minimal to mild form of endometriosis. The success of COH+IUI in moderate to severe cases are very low and hence should not be offered in this subgroup patients. A recent retrospective report demonstrated poorer efficacy of post-operative COH with IUI in endometriosis, where the cumulative pregnancy rate after 6 cycles COH+IUI was 45% and 42% in control in mild to moderate endometriosis. It was 10% and 20% respectively in advanced endometriosis.[10] It has been concluded by different studies that up to 3 cycles of COH with IUI is optimal regimen. 3 cycles of COH with IUI regimen as seen in different studies.[11,12]

## CONCLUSION

After surgical treatment of endometriosis, COH with IUI could be reserved for infertile patients with minimal or mild endometriosis who wish to plan for pregnancy immediately without a waiting period and does not want expected management. A maximum of 3 cycles could be offered to this sub group failing which IVF-ET (In vitro fertilization and embryo transfer) should be offered. Patients with stage III/IV endometriosis should not be offered COH with IUI as a treatment option. The patient should be counselled regarding the success rate of COH with IUI in the particular stage of endometriosis and the cost effectiveness of the treatment compared to IVF-ET. This will help us to achieve a better patient satisfaction and results in the treatment of infertility in endometriosis.

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## REFERENCES

1. Kennedy S. ESHRE Guidelines for the diagnosis & treatment of endometriosis. Hum Reprod. 2005;20: 2698-704.
2. Meuleman C. High prevalence of endometriosis in infertile women with normal ovulation and normospermic partners. Fertil Steril. 2009;92:68-74.
3. Schwartz D, Mayaux MJ. Female fecundity as function of age: results of Artificial Insemination in 2193 Nulliparous women with Azoospermic husbands. N Eng J Med. 1982;306(7):404-6.
4. Hughes EG. A quantitative overview of controlled trials in endometriosis associated infertility. Fertil Steril. 1993;59:963-70.
5. Fedele L, Marchini M, Bianchi S, Dorta M, Arcaini L, Fontana PE. Structural and ultrastructural defects in preovulatory endometrium of normo-ovulating infertie women with minimal or mild endometriosis. Fertil Steril. 1990;53:989-93.
6. Tummon IS, Maclin VM, Radwanska E, Binor Z, Dmowski WP. Occult ovulatory dysfunction in women with minimal endometriosis or unexplained infertility. Fertil Steril. 1988;50:716-20.
7. Vollenhoven B, Selub M, Davidson O, Lefkow H, Henault M, Serpa N, Hung TT. Treating infertility. Controlled ovarian hyperstimulation using human menopausal gonadotropin in combination with intrauterine insemination. J Reprod Med. 1996; 41:658-64.
8. Geber S, Paraschos T, Atkinson G, Margara R, Winston RML. Results of IVF in patients with endometriosis: the severity of the disease does not affect outcome, or the incidence of miscarriage. Hum Reprod. 1995;10:1507-11.

9. Attila K. Pregnancy Rate after controlled ovarian hyperstimulation and intrauterine insemination for the treatment of endometriosis following surgery. BioMed Res Int. 2015.
10. Gandhi AR, Carvalho LF, Nutter B, Falcone T. Determining the fertility benefit of controlled ovarian hyperstimulation with intrauterine inseminatuion after operative laparoscopy in patients with endometriosis. J Minim Invasive Gynecol. 2014;21:101-8.
11. Aboulghar M, Mansour R, Serour G, Abdrazek A, Amin Y, Rhodes C. Controlled ovarian hyperstimulation and intrauterine insemination for treatment of unexplained infertility should be limited to a maximum of three trials. Fertil Steril. 2001;75: 88-91.
12. Dmowski WP, Pry M., Ding J., Rana N. Cycle specific and cumulative fecundity in patients with endometrioisi who are undergoing controlled ovarian hyperstimulation- intrauterine insemination or in vitro fertilization- embryo transfer. Fertil Steril. 2002;78: 750-6.

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