

Research Article

A Study on the Impact of Endoscopic Myomectomy on Reproductive Outcomes of Assisted Reproductive Technology

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A B S T R A C T

Introduction: Uterine fibroids (myomas or leiomyomas) are the most common benign tumours in women of reproductive age. They have varied clinical presentations ranging from being asymptomatic to being a major source of clinical morbidity. The presence of uterine fibroids has been linked to fertility problems.

Aims: The primary objective of the study is to evaluate the effect of endoscopic myomectomy on IVF outcomes in patients with fibroids in terms of pregnancy rate, implantation rate, and ongoing pregnancy rate. Miscarriage rates and ectopic and heterotopic pregnancy rates were also studied as secondary objectives.

Method: This single-centre, retrospective observational study was conducted on patients with uterine myoma who visited Chennai Fertility Centre and Research Institute, Chennai for infertility treatment during the period of June 2013 to June 2022. Statistical analysis used The collected data was presented as a mean and standard deviation, frequency, or percentage. Pearson's chi-square test was used to assess the association between IVF outcome and variables. Tests that were statistically significant at < 0.05 were considered. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software version 24.0.

Results: The results showed higher ongoing pregnancy rates in the study group compared to the control group (68.89% vs. 42.2%) with a statistically significant difference in the p value (0.011).

Conclusion: It can be concluded that endoscopic myomectomy, either laparoscopic or hysteroscopic, can be used as a treatment for submucosal and large (> 4 cm) intramural fibroids and can improve the clinical pregnancy rate and cumulative implantation rate of infertile patients with fibroids.

Keywords: Fibroids, Infertility, In Vitro Fertilisation, Myoma, Implantation, Laparoscopy, Hysteroscopy, Pregnancy Rate

Introduction

Although they may be asymptomatic, uterine fibroids (also known as myomas or leiomyomas) are the most prevalent benign tumours in women of reproductive age and a significant cause of clinical morbidity.^{1,2} Fibroids are masses of extracellular matrix rich in collagen, fibronectin, and proteoglycan that develop from the smooth muscle of the myometrium.^{1,3} The prevalence of fibroids varies from 4.5% to 68.6% depending on study populations and diagnostic techniques.⁴ About 25% of women in the reproductive age group can experience considerable symptoms from fibroids.⁴ Its prevalence in India has been estimated at 37.65% in rural areas and 24% in urban areas.⁵ Numerous research has been conducted to determine the relationship between uterine fibroids and infertility because the existence of fibroids has been linked to issues with conception. The treatment of fibroids in infertility should be individualised based on the symptoms, size, and location of the fibroids. Myomectomy can be performed by laparotomy, minilaparotomy, laparoscopy, hysteroscopy, or a combination of these according to the number, size, and location of fibroids.⁶ The laparoscopic approach has been known to have several benefits and is considered superior to laparotomy for myomectomy in terms of less blood loss, diminished postoperative pain, fewer overall complications, faster recovery, and a significant cosmetic advantage. Hysteroscopic myomectomy can be considered the first-line conservative surgical therapy for the management of symptomatic intracavitary submucosal fibroids.⁷ Despite the high prevalence of fibroids in the Asian population, extensive evidence on the effects of laparoscopic myomectomy on pregnancy rates post-in vitro fertilisation (IVF) treatment is lacking. The purpose of the current retrospective study was to determine whether the location of uterine fibroids in women may affect their ability to reproduce and whether removing the fibroid before fertilisation may increase the likelihood of pregnancy and its maintenance.

The aim of the study was to evaluate the effect of endoscopic myomectomy on IVF outcomes in patients with intramural and submucosal fibroids in terms of pregnancy rate, implantation rate, and ongoing pregnancy rate. Miscarriage rates and ectopic and heterotopic pregnancy rates were also studied as secondary objectives.

Subjects and Methods

A single-centre, retrospective observational study was performed at the Chennai Fertility Centre and Research Institute Chennai, Tamil Nadu. It was duly approved by the institutional human ethics committee (approval certificate number CFCRI/IHEC/APL/2023/003). The study sample consisted of 90 patients with a history of infertility along with the presence of uterine myoma who came for IVF

treatment during the period of June 2013 to June 2022. They were further divided into study and control groups depending on who underwent endoscopic myomectomy. The recruited patients were confirmed to have uterine myoma by transvaginal ultrasound (TVUS). Prior to IVF treatment, a transvaginal ultrasound was performed. Endometrial thickness and abnormalities of the uterus were assessed by viewing the uterus in the longitudinal and transverse planes. Patients who underwent myomectomy and then IVF for the given duration were included in the study. The control group comprised 45 patients with fibroid uterus and infertility who underwent IVF without myomectomy. Cases who underwent myomectomy were given injections of leuprolide during the postoperative period, and IVF was done three months later. For both cases and the control group, the antagonist protocol was followed. In this protocol, rFSH in a dose of 150-300 IU was given from day 3 of menses, and an injection of Cetrotide 0.25 mg was added when the lead follicle size was 11 mm or more. Leuprolide 2 mg was used to trigger ovulation, and oocyte retrieval was performed 34–36 hours later. For endometrial preparation, downregulation by leuprolide followed by exogenous oestrogen followed by progesterone supplementation was performed. Frozen-thawed embryo transfer was performed at the blastocyst stage on day 5. Individual patient records were examined, and information regarding each patient's demographics, current symptoms, number and outcome of prior pregnancies, preoperative diagnostic techniques and their findings, operative details and complications, and post-operative reproductive outcomes were all analysed. The primary outcomes studied were pregnancy rate, implantation rate, and ongoing pregnancy rate. Secondary outcomes studied were miscarriage rate, ectopic pregnancy, and heterotopic pregnancy.

The subjects included in this study belonged to the age group of 21 to 45 years, and with the clinical findings of submucous or intramural fibroids distorting the cavity, intramural fibroid of more than 4 cm size, multiple fibroids and a previous history of recurrent abortion. Patients with broad ligament fibroid and subserous fibroid, adenomyoma, male factor infertility and other congenital uterine anomalies were excluded.

Laparoscopic and Hysteroscopic Myomectomy Surgical Technique Used

Laparoscopic myomectomy was performed using a routine technique, which consisted of three stages: enucleation, re-approximation of the myoma bed, and specimen extraction. The myometrium was incised using a harmonic scalpel or monopolar electrocautery, either in a transverse or longitudinal fashion, according to the position of the myoma. The myoma was enucleated using traction and countertraction, along with bipolar energy. The myometrium was closed using an absorbable V Loc

suture 1-0. Myoma extraction was then done using a morcellator inside a bag so that there was no spillage inside the peritoneal cavity.

Hysteroscopic myomectomy was done for submucosal myomas. When a myoma was less than 2 cm in diameter, its base was cut out at the endometrial level, and the myoma was then removed with a loop or blindly with a curette. A progressive regression was used for fibroids greater than 2 cm, moving from the myoma's surface to the endometrium. The myoma's intracavitary layer up to the myometrium was resected.

Statistical Analysis

The collected data was presented as a mean and standard deviation, frequency, or percentage. The association between the results of IVF and various covariates was evaluated using Pearson's chi-square test. Tests that were statistically significant at < 0.05 were considered. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software version 24.0.

Results

The study group and controls were comparable with respect to clinical characteristics, which are shown in Table 1. Grades of myoma are given in Table 2. Analysis of demographic variants showed that the mean age of both groups was comparable, with the mean age being 38.16 years in the study group and 36.51 years in the control group. The difference in BMI was significant in both groups (p value: 0.02). In the myomectomy group, the majority of the cases, 82.2%, underwent laparoscopic myomectomy, and 15.6% underwent hysteroscopic myomectomy. In one case, laparoscopic myomectomy was followed by hysteroscopic myomectomy. Out of 45 patients, 9 had submucosal fibroids (SM), 35 had intramural fibroids (IM), and 1 had a hybrid submucosal–intramural fibroid (SM-IM). Amongst 45 patients in the non-myomectomy group, 2 had SM fibroids, 41 had IM fibroids, and the remaining 2 had IM-SM fibroids. As per FIGO grading of myoma, Grade 4 myoma was the most common in both the study group and controls (48.89% and 60%, respectively), followed by Grade 2 and 3 myoma in the study group and Grade 3 in controls. 36 out of 45 patients who underwent myomectomy became pregnant after the surgery. According to this study, women who had surgical fibroid removal had a greater pregnancy rate than women who did not have surgery. Compared to the control group, the study group has a greater pregnancy rate (80% vs 60%), with a p value < 0.038. The clinical pregnancy rate was approximately 73.3% in the study group, while it was 53.33% in controls, which was significantly higher with a p value of 0.017. The study group also had a higher implantation rate than the controls, with a mean of 83.59 and 71.97 respectively, and a p value of 0.017. The present study analysed the ongoing

pregnancy rates among the myomectomy group, which was 68.89% compared to 42.2% in the control group, with a p value of 0.011. In the present study, the miscarriage and ectopic pregnancy rates were similar in both groups. The pregnancy outcomes are shown in Table 3.

Table 1. Clinical Characteristics of Cases and Controls

Clinical Characteristics		Cases (N = 45)	Controls (N = 45)	p Value
		Mean (SD)/ n (%)		
Mean (SD)				
Age		38.16 (4.55)	36.51 (4.48)	0.080
BMI		27.76 (4.08)	29.55 (2.99)	0.020
Duration of infertility		9.52 (5.81)	11.2 (6.00)	0.810
n (%)				
Previous IVF failures		14 (31.11)	16 (35.56)	0.650
Type of infertility	Primary	26 (57.77)	30 (66.66)	0.384
	Secondary	19 (42.22)	15 (33.33)	
Type of myoma	Intramural	35 (77.78)	41 (91.11)	0.070
	Submucosal	9 (20.00)	2 (4.44)	
	Intramural + submucosal	1 (2.22)	2 (4.44)	

Table 2. Comparison of Grades of Myoma among Cases and Controls

Myoma Grade	Group		Total
	Cases n (%)	Controls n (%)	
1	1 (2.22)	0 (0.00)	1
2	8 (17.77)	4 (8.89)	12
2 & 4	1 (2.22)	0 (0.00)	1
3	8 (17.77)	13 (28.89)	21
3 & 4	2 (4.44)	0 (0.00)	2
4	22 (48.89)	27 (60.00)	49
4 & 2	1 (2.22)	0 (0.00)	1
4 & 3	0 (0.00)	1 (2.22)	1
5	2 (4.44)	0 (0.00)	2
Total	45	45	90

Table 3. Pregnancy Outcomes in Cases and Controls

Pregnancy Outcomes	Cases	Controls	p Value
	Mean (SD)/ n (%)		
	Mean (SD)		
Implantation rate	83.59 (17.48)	71.97 (16.57)	0.017
	n (%)		
Clinical pregnancy rate	33 (73.3)	24 (53.33)	0.017
Ongoing pregnancy rate	31 (68.89)	19 (42.20)	0.010
Miscarriage rate	4 (8.89)	7 (15.56)	0.334
Ectopic pregnancy rate	1 (2.22)	3 (6.67)	0.306

Discussion

The development and maintenance of early pregnancy may be impacted by submucosal (SM), intramural (IM), and mixed SM-IM fibroids, which have been known to cause uterine cavity distortion. This study supports the evidence of the valuable role of endoscopic surgery for selected categories of myomas before the IVF cycle. Similar to our study, higher pregnancy and clinical pregnancy rates have also been reported by Dubuisson et al.⁸ and Wang et al.⁹. Horne and Critchley, in their study, obtained a significantly higher implantation rate in subjects undergoing myomectomy.¹⁰ The statistically significant higher ongoing pregnancy rates confirm the findings of Yoshino et al. who suggested that decreased pregnancy rates in the presence of myoma are linked to abnormal uterine peristalsis, and hence myomectomy can be beneficial in such cases.¹¹ In 19 observational studies that included a total of 6,087 IVF cycles, Sunkara et al. conducted a systematic review and meta-analysis on the most contentious topic of the association between intramural fibroid not altering the cavity and IVF outcome.¹² Following IVF treatment, women with non-cavity distorting intramural fibroids had significantly lower live birth rates (RR 0.79; 95% CI 0.70–0.88) and clinical pregnancy rates (RR 0.85; 95% CI 0.77–0.94) than women without fibroids. Casini et al. examined the effects of myomectomy on fertility in a prospective controlled trial.¹³ They randomly assigned 181 women who had submucosal, intramural, and subserosal fibroids to receive either surgical treatment or expectant care, and they reported the pregnancy rates in each grouping after timed sexual intercourse. The authors discovered that women with submucosal fibroids as well as those who had both submucosal and intramural fibroids experienced statistically significantly greater pregnancy rates following myomectomy. The success of myomectomy prior to IVF has been supported by a further comparison study by Bulletti

et al.¹⁴ Patients having at least one lesion with a mean diameter of 5 cm who were chosen for the operation and were found to have intramural-subserosal fibroids were included. For women who underwent surgery vs those who did not, the cumulative delivery rate was 25 and 12%, respectively. The miscarriage rate after surgery was 26% compared to 62% before hysteroscopic myomectomy for women who had a prior miscarriage, according to a prospective cohort study by Shokeir.¹⁵ In this study, 72% of women with primary infertility conceived within 4 years of surgery and without further intervention. In our study, however, the miscarriage rate was not different between the two groups, probably due to the small sample size. Rikhraj et al. included 15 trials with 5029 patients in one of their most recent meta-analyses.¹⁶ Patients with non-cavity-distorting intramural fibroids had 32% lower odds of clinical pregnancy and 44% lower odds of live birth (estimated average odds ratio [OR] = 0.56, 95% confidence interval [CI] = 0.46–0.69). Live birth rates and clinic pregnancy rates were considerably lower in subgroup analyses of women with exclusively intramural fibroids. Numerous mechanisms, including anatomical distortion of the uterine cavity and subsequent changes to endometrial function, functional changes like increased uterine peristalsis and impairment of the endometrial and myometrial blood supply, changes to the local hormone milieu, and paracrine molecular changes induced by fibroids, which could impair gamete transport, are all possible ways by which fibroids can reduce fertility.^{10,11} When carried out by a skilled surgeon, endoscopic myomectomy can be regarded as a safe surgery with a very low failure rate, thereby increasing the reproductive outcomes in infertility cases with fibroid uteri.

Limitations

The main limitations of the current study were its limited sample size, single-centre design, and retrospective nature.

The best surgical approach and the intraoperative variables that should be noted and discussed for postoperative management, both require additional investigation using well-planned prospective clinical trials. The role of myomectomy in intramural fibroids < 4 cm needs to be evaluated in adequately powered prospective studies.

Conclusion

Endoscopic myomectomy, either laparoscopic or hysteroscopic, can be used as a treatment for submucosal and large (> 4 cm) intramural fibroids and could improve the clinical pregnancy rate and cumulative implantation rate of infertile patients with fibroids. Our study demonstrates a promising clinical pregnancy outcome after endoscopic myomectomy in the Asian population. The first-line conservative surgical treatment for the management of symptomatic intracavitary fibroids should be hysteroscopic myomectomy. Also, our study demonstrates that IVF treatment can be safely started immediately, 3 months post-myomectomy.

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Conflict of Interest: None

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