Research Article

Reproductive Performance After Hysteroscopic MyomectomyFor Myoma Associated Reproductive Failure

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Abstract
Objective: To assess the reproductive outcome in patients undergoing hysteroscopic myomectomy for reproductive failure. **Methods:** Prospective observational study. Setting: conducted in Endoscopy unit, OB/GYN department, Minia Maternity University Hospital, Minia, Egypt.Sixty-three patients with submucosal fibroids associated with reproductive failure (primary infertility, secondary infertility, recurrent pregnancy losses and/or preterm deliveries). Intervention: Hysteroscopic resection using bipolar versapoint resectoscope under general anesthesia. Outcome measure(s): Reproductive outcome during the follow-up period. **Results:** The mean ± SD duration of follow-up was ١٥.٣٦ ± ٩.٨٣ months. Twenty eight (٤٤.٤٪) patients had primary infertility, ١٢ (١٩٪) patients with secondary infertility, ٣ (٤.٨٪) patients had recurrent first trimester miscarriage, ٥ (٨٪) patients had recurrent second trimester miscarriage, and ١٥ (٢٣٪) patients had preterm delivery. The mean ± SD duration of the procedure was ٣٢ ± ٩.٢ min, and the mean ± SD length of hospital stay was ١٠.٥ ± ٢.٦ hrs. Operative complications were minimal including ٣ cases with cervical laceration during cervical dilatation. Postoperative complications were minimal and didn't require extra hospitalization. Hysteroscopic myomectomy significantly improved menstrual pattern in ٧٥.٨٪ of patients complaining of menorrhagia (p=٠.٠٠١). There was statistically significant improvement in the reproductive outcome after the procedure (p=٠.٠٠٠١). Two patients (٣.٢٪) ended in first trimester miscarriage, ٢/٦٣ (٣.٢٪) had second trimester miscarriage, ١١/٦٣ patients (١٧.٤٪) ended in preterm labor, while ٤٦/٦٣ (٧٣٪) had reached to term delivery. There was statistically significant difference in the pregnancy rate, live birth rate and gestational age before and after the procedure (p= ٠.٠٠٠١, ٠.٠٠٠١, ٠.٠٠١ respectively). **Conclusion:** Hysteroscopic myomectomy using the bipolar versapoint resectoscope is a safe and effective therapeutic modality for patients with submucous fibroid and associated reproductive failure up to ٣٦ months follow-up.

Key words: Submucous fibroid, Hysteroscopic myomectomy and Reproductive outcome.

Introduction
Uterine fibroids are the most common benign solid tumors found in the female genital tract. They occur in ٢٠–٢٥٪ of women of reproductive age causing ٣–٥٪ of gynecology consultations[١,٢].

Reproductive outcome with fibroids depends on the site of the tumor; submucosal fibroids have a major impact on fertility more than intramural and subserous types[٣,٤].

Submucous fibroids are characterized by either clinical symptoms such asmenorrhagia and colicky dysmenorrheal[٥], or reproductive complications as infertility, repeated miscarriage, preterm labor, abnormal presentation, post-partum hemorrhage and puerperal complications [٦].

Abdominal myomectomy for submucous fibroids requires the opening of the uterine cavity that results in altering the likelihood of subsequent conception or it may interfere with vaginal deliveries. Furthermore, such approach may cause post-operative pelvic

adhesions affecting any future pregnancy[٧].

Hysteroscopic surgery has revolutionized the management of submucosal fibroid allowing access and resection from within the uterine cavity [٨, ٩].

Neuwirth and Amin[١٠] removed a submucosal fibroid using urological resectoscope in ١٩٧٦. Thanks to advances in instruments and the refining of techniques, hysteroscopic myomectomy has become the standard minimally invasive surgical procedure for treating fibroids entirely or mostly located within the uterine cavity[١١-١٣].

The aim of this study was to assess the reproductive outcome in patients undergoing hysteroscopic myomectomy for reproductive failure.

Subjects and Methods

This prospective study was conducted at the endoscopy unit of the Obstetrics and Gynecology Department, I Maternity University Hospital, Faculty of MedicIMinia University, between October ٢٠٠٧ and July ٢٠١١. The study was approved by scientific ethical committee of the depart-ment of Obstetrics and Gynecology, on August ٢٠٠٧, and the Institutional Review Board of the University Hospital-Quality control unit of the Faculty of Iine, Minia University on September ٢٠٠٧. The study protocol was explained to all patients and an informed written consent was taken from each patient before enrollment.

The study included ٦٣ patients with sub mucosal fibroids associated with reproductive failure (primary infertility, secondary infertility, recurrent pregnancy losses and/or preterm deliveries). Primary infertility was defined as failure to conceive after ١٢ months of regular marital life. Secondary infertility was defined as the inability to conceive after ١٢ months of contraceptive-free intercourse after having already conceived at least once. Recurrent pregnancy loss was defined as three or more consecutive spontaneous pregnancy losses before ١٣ weeks gestation (recurrent first trimester miscarriage) or between ١٣ and ٢٤ weeks (recurrent second trimester miscarriage). Preterm delivery was defined as delivery between ٢٤ and ٣٧ weeks.

All patients with submucosal uterine fibroids that affect their reproductive career and with no contraindication for pregnancy or surgery were invited to participate in the study. Patients with the following criteria were excluded from the study: age > ٣٧ years old, other causes of reproductive failure as male factor, ovulatory disorder, tubal block, pelvic adhesion diagnosed by laparoscopy and PID. Patients with less than ١٢ months of follow-up were also excluded from this study.

All of the patients and their partners underwent thorough history taking, systematic clinical examination and local pelvic examination, routine laboratory investigations as CBC, liver & kidney functions to exclude general disease contraindicating pregnancy or surgery. All of the patients, and their partners had complete infertility investigations, including sexually transmitted disease work-up, semen analysis, endocrine evaluation as necessary, assessment of ovulation, and recurrent miscarriage work-up.

The work-up to diagnose submucosal fibroid included hysterosalpingography (HSG), pelvic ultrasound (using ٧.٥ MHz intracavitary probe, Sonoace ٩٩٠٠, Medison, Seoul, Korea) with or without saline infusion into the endometrial cavity (sonohysterography), and office hysteroscopy (Versascope of Gyncare, USA, with diameter of ٢.٩ mm). Sometimes magnetic resonance imaging (MRI) and diagnostic laparoscopy were done as a part of routine infertility work-up.

Outcome measures:

Primary outcome parameter was reproductive outcome (number and duration of pregnancies, number of life births and interval between the intervention and diagnosis of pregnancy). The secondary outcome parameters were the number and duration of intervention and type of intra- and post-operative complications in order to gain information on the safety of the procedure.

Procedure:
All procedures were performed as in-patient surgery under general anesthesia during the follicular phase of the menstrual cycle. No hormonal preparations were used prior to the procedure but we used intra-vaginal misoprostol ٤٠٠ mcg for cervical ripening ٢-٤ hours before the procedure. The cervix was grasped with a volsellum and dilated up-to Hegar ٩. The uterine cavity was distended with ٠.٩ normal saline at an inflow pressure of ٦٠–٩٠ mmHg, using a hysterometer to adjust the pressure of the follow, the amount of fluid used and the deficit after the operation. A bipolar loop resecting electrode (٤mm) was connected to the bipolar resectoscopic system (GYNECARE VERSAPOINT^{TM}, USA) with ٢٧Fr (٩mm) outer sheath diameter, ٢٤Fr (٨mm) inner sheath diameter, ٢٠٠mm working length, and a passive working element. A ١٢° or ٣٠° wide-angle ٤.٠ mm rod lens STORZ mount hysteroscopy was used. In ٥٧ (٩٠.٥٪) patients the fibroid was intracavitary[١٤] and the procedure was complete in one session, while ٦ (٩.٥٪) patients had intramural fibroid class I with largest diameter in the cavity[١٤] that required second step procedure as described by Loffer[١٥]. The second step was done following the next menstruation using the same operative technique by means of slicing of the residual component of the fibroid, which has now become intra-cavitary. This series didn't include any patients with more than one submucous fibroid. A second look office hysteroscopy was performed in all patients following the next menstruation using the ٣٠° versascope (Gynecare, USA), with a diameter of ٢.٩ mm without anesthesia as an outpatient procedure to asses if there are any adhesions. If adhesions were found, they were lysed in the same setting.

The operative time was recorded for each patient. All intra or post-operative complications as hemorrhage, perforation or incomplete resection were recorded. Data on the subsequent reproductive performance of each patient were recorded.

Statistical Analysis
Data were statistically described in terms of range, mean ± standard deviation (±SD), median, frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables between different groups in the present study was done using Mann Whitney U test for independent samples. For comparing categorical data, Chi square test was performed. Exact test was used instead when the expected frequency is less than ٥. Accuracy was represented using the terms sensitivity and specificity. A probability values (p value) less than ٠.٠٥ were considered statistically significant.
Statistical analysis
All statistical calculations were done using computer programs Microsoft Excel version ٢٠١١ (Microsoft Corporation, NY, USA), SPSS (Statistical Package for the Social Science; SPSS; Inc., Chicago, IL, USA) and Arcus Quick Stat (Bio-medical version, Addison Wesley Longman Ltd, USA) statistical-program.

Results
A total sixty-three patients were included in the study. The mean ± SD age was ٢٨.٢ ± ٤.٨ years, the mean ± SD gravidity was ١.٥ ± ٢, and the mean ± SD duration of follow-up was ١٥.٣٦ ± ٩.٨٣ months. The demographic characteristics of the patients are shown in table ١.

٢٨(٤٤.٤٪) patients had primary infertility, ١٢(١٩٪) patients with secondary infertility, ٣(٤.٨٪) patients had recurrent first trimester miscarriage, ٥(٨٪) patients had recurrent second trimester miscarriage, and ١٥(٢٣٪) patients had preterm delivery (table ٣).

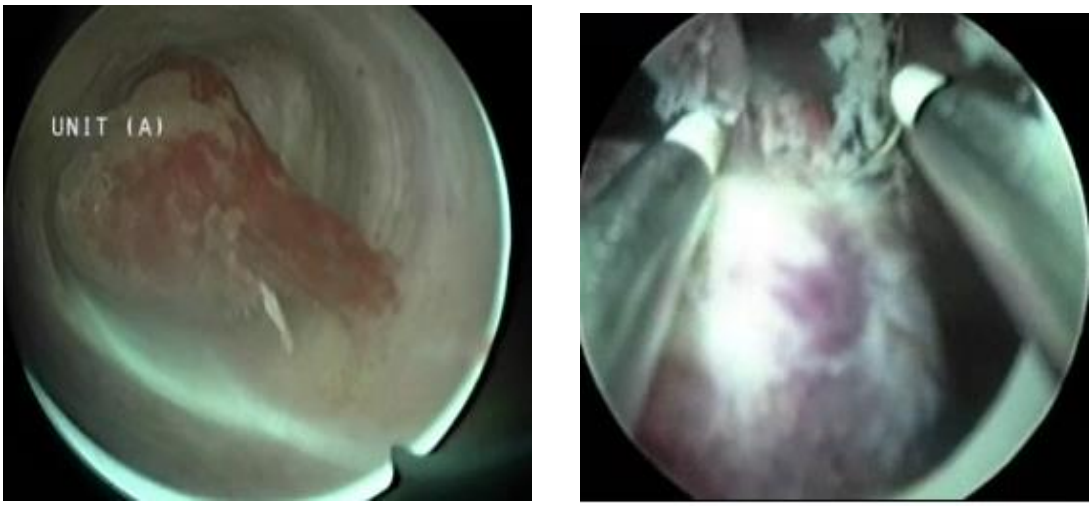
٥٧(٩٠.٥٪) cases with intracavitary fibroid had complete operative procedure in the same setting while ٦(٩.٥٪) patients had submucous fibroid with intramural extension that required two-steps procedure as described by Loffer (١٩٩٠).

The operative and post-operative data are given in table ٢. The mean ± SD duration of the procedure was ٣٢±٩.٢ min (range ٦–٥٥ min), and the mean ± SD length of hospital stay was ١٠.٥±٢.٦ hours (range ٦–١٤ hours). Operative complications were minimal including ٣ cases with cervical

laceration during cervical dilatation. Intra-operative blood loss was minimal in ٥٤ (٨٥.٧٪) cases and moderate in ٩(١٤.٣٪) patients. Postoperative complications didn't require extra hospitalization. Five patients (٨٪) had type I intra-uterine adhesions according to Modified European Society of Hystero-scopy (ESH) and European Society of Gynecological Endoscopy (ESGE) classifi-cation of intrauterine adhesions[١٦], all adhesions were lysed in the same setting.

Table ١: Demographic characteristics of patients

Demographic characteristics		
Age (years)	Range (mean ± SD)	٢٠ - ٣٧ (٢٨.٢ ± ٤.٨)
Gravidity	Range (mean ± SD)	٠ - ٧ (١.٥ ± ٢)
Menstrual pattern **Eumenorrhea** **Menorrhagia**	 N (%) N (%)	 ٣٤ (٥٤٪) ٢٩ (٤٦٪)
Diameter of fibroid (mm)	Range (mean ± SD)	٢٠ – ٥٠ (٣٢.٦ ± ٤.٣)
Site of submucous fibroid **Intracavitary** **Intramural with largest diameter in cavity**	 N (%) N (%)	 ٥٧ (٩٠.٥٪) ٦ (٩.٥٪)
Duration of follow-up (months)	Range (mean ± SD)	١٢ - ٣٦(١٥.٣٦ ± ٤.٨٣)



Figures (١): A) resection of large intracavitary myoma, b) intracavitary fibroid in patient presented with primary infertility.

Table ٢: Operative and post-operative data of hysteroscopic myomectomy:

Operative and post-operative data		
Operative time (min)	Range (mean ± SD)	٦ – ٥٥ (٣٢ ± ٩.٢)
Hospital stay (hr)	Range (mean ± SD)	٦ – ١٤ (١٠.٥ ± ٢.٦)
Cervical laceration	N (%)	٣ (٤.٨٪)
Uterine perforation	N (%)	٠
Fluid overload	N (%)	٠
Blood loss **Mild** **Moderate** **Severe**	 N (%) N (%) N (%)	 ٥٤ (٨٥.٧٪) ٩ (١٤.٣٪) ٠
Post-operative pain		

None	N (%)	٤٨ (٧٦.٢٪)
Mild	N (%)	١٥ (٢٣.٨٪)
Severe	N (%)	٠
Post-operative fever	N (%)	٤ (٦.٣٪)

In the current study, hysteroscopic myomectomy significantly improved menstrual pattern in ٧٥.٨٪ of patients complaining of menorrhagia, where only ٧/٦٣ (١١.١٪) patients had persistent menorrhagia after the procedure compared to ٢٩/٦٣ (٤٦٪) with menorrhagia before the procedure (p=٠.٠٠٢) (table ٣).

The mean time until the first conception was ٩.٤ months (range: ٢–٢٦ months) after the operation. Thirteen women got pregnant twice during the study period. There was statistically significant improvement in the reproductive outcome after the procedure (p=٠.٠٠٠١). Two patients (٣.٢٪) ended in first trimester miscarriage, ٢/٦٣ (٣.٢٪) had second trimester miscarriage, ١١/٦٣ patients (١٧.٤٪) ended in preterm labor, while ٤٦/٦٣ (٧٣٪) had reached to term delivery (table ٣). There was statistically significant difference in the pregnancy rate, live birth rate and gestational age before and after the procedure (p= ٠.٠٠٠١, ٠.٠٠٠١, ٠.٠٠١ respectively) (table ٤).

Table ٣: Reproductive outcome before and after hysteroscopic myomectomy:

Variable	Before myomectomy	After myomectomy	P value
• Menstrual pattern Eumenorrhea Menorhagia	 ٣٤ (٥٤٪) ٢٩ (٤٦٪)	 ٥٦ (٨٨.٩٪) ٧ (١١.١٪)	 ٠.٠٠١
• Reproductive outcome			
١ry infertility	٢٨ (٤٤.٤٪)	٢ (٣.٢٪)	٠.٠٠٠١
٢ry infertility	١٢ (١٩٪)	٠	
١st trimester miscarriage	٣ (٤.٨٪)	٢ (٣.٢٪)	
٢nd trimester miscarriage	٥ (٨٪)	٢ (٣.٢٪)	
Pre-term labor	١٥ (٢٣.٨٪)	١١ (١٧.٤٪)	
Full-term delivery	٠	٤٦ (٧٣٪)	

Table ٤: Obstetric outcome before and after hysteroscopic myomectomy:

Variable	Before myomectomy	After myomectomy	P value
Clinical pregnancy rate (N, %)	٢٣/٦٣ (٣٦.٥٪)	٦١/٦٣ (٩٦.٨٪)	٠.٠٠٠١
Live birth rate (N, %)	٦/٦٣ (٩.٥٪)	٥٣/٦٣ (٨٤٪)	٠.٠٠٠١
Gestational age in weeks (range, mean ± SD)	٠-٤٠ (١٣.١٧±١٣.٦)	٠-٤٠ (٣٤.٣٣±٩.٤)	٠.٠٠١

Discussion

In the present study, the pregnancy rate after hysteroscopic myomectomy was ٦١/٦٣ (٩٦.٨٪), ٢/٦٣ patients (٣.٢٪) ended in first trimester miscarriage, ٢/٦٣ patients (٣.٢٪) had second trimester miscarriage, ١١/٦٣ patients (١٧.٤٪) ended in preterm labor, and ٤٦/١٤٧ patients (٧٣٪) had reached to term delivery. Live birth rate was ٨٤٪ (٥٣ out ٦٣), ٤٦ were full term pregnancy while the remaining ٧ cases were preterm labor. Previous studies reported pregnancy rates

following hysteroscopic myomectomy

ranging between ١٦.٧ to ٧٧٪[١٧-١٩].

This wide range may be due difference in sample size, patients' main complaints, fibroid properties (number, site, size, and presence of concomitant intramural fibroids) or range of postoperative follow-up period[٤]. The higher pregnancy rate in our study could be attributed to the inclusion of patients with: age less than ٣٧ years, single fibroid, no associated cause of infertility, and inclusion of fertile patients with pregnancy loss and/or preterm labor.

Fibroids are present in about ٥-١٠٪ of infertile patients[٢٠] however, they are found to be the sole identified factor in only ١-٢.٤٪ of the infertile patients[٢١-٢٤]. In the current study, ٤٠/٦٣ (٦٣.٤٪) of patients had infertility and all but two achieved pregnancy after the procedure. Although improved fertility rates after hysteroscopic myomectomy has been previously reported, there is absence of high quality evidence about the effects of hysteroscopic myomectomy on the management of infertile women; most of these studies were retrospective[١,٤,٦,٢٢,٢٥,٢٦]. Stamatellos et al.,[٢٧] have prospectively found that hysterosopic myo-mectomy improved fertility rates by ٥٧.١٪ for patients with type ٠ myoma and ٤٢.٨٪ for type ١ myomas. Interestingly, in patients with type ٢ fibroids fertility rate did not increase, in contrast with patients with type ٢ fibroids who received expectant mana-gement (control group).

In the current study, the miscarriage rate after and before the procedure was ٢/٦٣ (٣.٢٪) vs ٣/٦٣ (٤.٨٪) for ١st trimester miscarriage and ٢/٦٣ (٣.٢٪) vs ٥/٦٣ (٨٪) for ٢nd trimester miscarriage respectively. A systematic review that analyzed ١١ controlled trials found that the spontaneous miscarriage rate in women with submucous fibroid undergoing IVF were higher than the rate in women with no fibroids[٢٨]. Studies have shown ٤٠-٦٠٪ reductions in miscarriage rates following abdominal myomectomy[١١,٢٩,٣٠]. However, studies comparing miscarriage rates before and after hysteroscopic myomectomies are sparse[٣١]. One study compared pre- and post-hysteroscopy miscarriage rates and found a reduction from ٧٣.١ to ٢٦٪[٣٦]. Other studies have reported only post-operative miscarriage rates ٨–٣٢٪ [٦, ١١, ٣٢].

In the present study, the mean surgery to conception time span was ٩.٤ months. This short interval till conception has also been previously reported[١,٣٣]. It is therefore strongly recommended that patients should attempt to conceive soon after the procedure[١].

Hysteroscopic myomectomy is an ideal option for management of submucous fibroid induced menorrhagia with a success rate ranging from ٧٠ to ٩٩٪[١٣]. Varma et al.,[٣٤] reported improved menstrual symptoms and patient satisfaction by ٩١٪ and ٨٦٪, respectively with mean follow-up of ٢.٦ years. In the present study hysteroscopic myomectomy improved menstrual pattern in ٧٥.٨٪ of patients complaining of menorrhagia where ٧/٦٣ patients (١١.١٪) with menorrhagia after the procedure vs ٢٩/٦٣ patients (٤٦٪) before the procedure (p= ٠.٠٠١). Usually the success rate declines as the follow-up period increases and failure rates could be caused by the presence of other dysfunctional factors as a cause of menorrhagia[١٣], hidden or missed fibroids in other sites, the presence of adenomyosis and the incomplete treatment of partially intra-mural submucous fibroids[٣٥]. Best results of controlling menorrhagia are accomplished when hysteroscopic myomectomy is com-bined with endometrial ablation in women with no desire for further pregnancies, which leads to an amenorrhoic status in up to ٩٥.٥٪ of patients[٣٦].

Our results show that operative complications were minimal including ٣ cases with cervical laceration during cervical dilatation with no uterine perforation or fluid overload and post-operative complications didn't require extra hospitalization. Similar results have been previously reported[١,٣٦] and it has been concluded that hysteroscopic resection of submucous fibroid is a safe procedure[١, ١٨, ٣٦].

In conclusion, hysteroscopic myomectomy using the bipolar versapoint resectoscope is a safe and effective therapeutic modality for

patients with submucous fibroid and associated reproductive failure up to ٣٦ months follow-up.

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