

Reproductive outcome of septate uterus following hysteroscopic septum resection

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Abstract: Objective: to evaluate the reproductive outcome following hysteroscopic Septumresection in patients with septate uterus complicated by recurrent pregnant loss, infertility and bad obstetric history. **Study Design**
Reproductive Outcome: Material and Method hysteroscopic Septum resection was Performed on 26 patients with history of either recurrent pregnant loss, BOH or, infertility. The Septum Resection Was Performed using monopolar system. Reproductive Performing Of these patients after system resecting was analysed; the main outcome measures were clinical pregnancy at live birth rate. **Results:** There was significant change in the results after, as (88, 46%) patients become pregnant, of them 3/23 (13, 04%) had habitual abortion, 2 patients (4, 34%) ended in preterm labour. 14/23 (60, 86%) had reached to term delivery with a total pregnancy loss of 5/23 (21, 73%) and pregnancy complication Occurred in of 5/23 (21, 73%). These result represent a statistically significant difference ($P < 0.05$), the mean gestational age, the mean neonatal weight at delivery Were significantly improved after hysteroscopicmetroplasty ($P < 0.05$). There were no intraoperative or postoperative complications, and complete removed of the septum was achieved in 21 patients (80, 67), a residual ' septum was found in 5 'women (19, 23), and a 2nd intervention was done in only 2 patients (7,69) with a residual septum $> 1\text{cm}$ using office hysteroscopy. **Conclusion:** metreoplasty in infertile women with septate uterus is effective and safe procedure with a subsequent pregnancy rate of (55.88%) and a life birth rate of (64.7%).

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1. Introduction

Incomplete resorption of the Mullerian duct during embryogenesis leads to Mullerian anomalies which may alter the reproductive outcome of the patients. The mean incidence of uterine defects in the general population and in infertile women is 4.3% (1).

In patients with recurrent pregnancy loss, the incidence of uterine defects increases by 5-25%. (2), (3). Septate uterus [class V, American fertility classification (4)]. Is the most common congenital uterine anomaly, comprising approximately 55% of Mullerian duct anomalies (5).

A septate uterus is not a primary factor for infertility. (6) Nearly 40% of patients with septate uterus have reproductive failure, obstetrical complications and an increased incidence of recurrent miscarriages. (7) Clinically, symptoms may range from being asymptomatic thus remaining undiagnosed, to the development of poor reproductive outcome. (8)

Accidental discovery of a uterine septum may sometimes occur during the evaluation of infertility. Uterine septum resection by a hysterolaparoscopic approach has been found to be beneficial with significant improvement in pregnancy rates post procedure. This has many advantages such as shorter operating and hospitalization periods, reduced risk of postoperative pelvic adhesions, low morbidity and an increased rate of vaginal delivery.

This retrospective study has been designed to evaluate the impact of hysteroscopic septum resection on the reproductive outcome of patients with a history of primary and secondary infertility.

The etiologies of infertile patients with uterine anomaly remain unclear.

The mechanisms of septate uterus causing early pregnancy loss and infertility have not been established. (9) In patients, the septum was identified during infertility evaluation.

We confirmed the diagnosis by performing diagnostic hysterolaparoscopy which enables us to operate and resect the-septum at the same sitting. Few studies also have stated that diagnostic hysterolaparoscopy is now accepted as the most effective 'approach.

Grimbizis and Kormanyos (1), (9) supports the use of hysteroscopic septum resection to improve pregnancy outcome in patients with a history of recurrent pregnancy loss (86%) and infertility (32%).

Those women with infertility after septum resection have an increased pregnancy rate (10).

A hysteroscopic guided septum resection not only eliminates an unsuitable site for implantation but also results in a better endometrial function, probably through revascularization of the connective tissue of the uterine fundus and significantly improves nidation (11).

The septum is thought to be composed of fibroelastic tissue with inadequate vascularization and altered relations between myometrial and endometrial vessels, thus exerting a negative effect on fetal placentation. (12) However, our findings are similar to those identified in a review of reproductive outcome before and after hysteroscopic septum resection.

In a literature survey, miscarriage and preterm delivery rates prior to septum resection were 88% and 9% respectively, and the live birth rate was only 3%. After septum resection, these rates were 14%, 6% and 80% respectively (13), (14).

Retrospectively examined the reproductive performance of infertile patients before and after septum resection and found that septum resection does not impair fertility, both in sub-septate and complete septum post procedure (1).

Our study also showed that hysteroscopic septum resection did not impair future fertility in cases of complete septum. We initiated treatment cycles two months post procedure in contrast to a larger study by Kormanyoset ah, (9) where treatment cycles were carried out after a minimum of four months. However, this interval between procedure and treatment cycle did not alter the pregnancy outcome.

Although the series were smaller in comparison, the pregnancy rates were significantly higher following septum resection.

Although the incidence is rare, there have been case reports of rupture post hysteroscopic septum resection in recent years (15).

2. Material and Methods

The reproductive efficiency in 26 patients with septate uterus who underwent hysteroscopic septum resection in department of Obstetrics and Gynaecology; Al azhar university hospital from January 2012 to September 2016.

Criteria for inclusion. No endocrine disorders; progesterone levels above 10 ng/ml in the mid-luteal phase; at least one fallopian tube patent demonstrated by hysterosalpingography; and partners with normal semen analysis.

Criteria for exclusion. Since we focused only on septate uterus in this study, we excluded the patients with associated genital or pelvic diseases (myomas, endometriosis, adhesions and pelvic inflammatory disease).

Women aged > 35 years were also excluded in order to avoid the chronological age related infertility.

Any other known cause of infertility was not included in this study.

The presenting complaints in these patients included secondary infertility (7/26, 27%) and unexplained infertility (19/26, 73%). Of the patients with secondary infertility (n=7), 4 (RPL) of them had

three to four previous first trimester pregnancy losses (83%) while the remaining three (BOH) had a previous cesarean section for preterm labor (at less than 28 weeks gestational age) which resulted in neonatal mortality. The gold standard for diagnosing uterine anomalies has always been hysterolaparoscopy.

The advantage of combining laparoscopy with hysteroscopy is well known. It offers a dual advantage of assessing the pelvis as well as the uterine cavity, aiding diagnosis and correlating or confirming findings crucial to therapy in cases of uterine anomalies.

If a suspicion is elicited in history or ultrasound of a septate uterus, this procedure which is considered as a gold standard in evaluation of infertile couples, enables us to, operate and resect the septum in a single sitting.

If a clear, pre procedure awareness is created and consent obtained for performance of the surgery, it avoids a second look and operative hysteroscopy, saving time and finances for the couple.

All operations were done as in-patient surgery. Not used any form of preoperative long term treatment with diazole or gonadotropin releasing hormone (GnRH) agonists. Septum resection performs under general anaesthesia by two surgeons combining hysteroscopy and laparoscopy. All procedures perform in the follicular phase of the menstrual cycle; within seven days after the end of menstruation. Under general anesthesia, hysteroscopic septum resection was performed using monopolar electro surgery. After cervical dilatation with Hegars dilators up to a width of 10mm; an operative hysteroscopic (Storz 10 mm fibreoptic resectoscope, Storz, Grab h) was inserted. The uterine cavity was distended with a 1.5% glycine solution with a continuous irrigating flow as the distension medium to avoid potential hyponatremia. The hysteroscopy hook was placed in contact with the septum and an incision was made perpendicular to the septum. The aim of the procedure was to accomplish a triangular and symmetrical uterine cavity.

Uterine septoplasty was performed under laparoscopic supervision.

Is assembled and the septum is divided into and from upward direction until complete visualization of both tubal ostia. Postoperative; all patient has intrauterine insertion of a 14 foley catheter with the balloon inflated to splint the uterus; this removed on the fifth postoperative day. Follow up done through outpatient clinic. And private infertility practice.

There is no complication such as uterine perforation, excessive bleeding, fluid overload or thermal injury. Postoperative evaluation and treatment of residual septum, when 2nd look office hysteroscopy demonstrated the presence of residual septum Statistics.

Statistics' analysis was performed by using the 2 test. The cumulative pregnancy rate for 72 months

follow up period was by Kaplan-Maier analysis. The comparison of pregnancy probability between three groups was evaluated by using log rank test and $p < 0.0$ was considered as statistically significant.

All septum were successfully resected with no hysteroscopic or anaesthetic complication demographic characteristics of the patients at the time initial pregnancy. Outcome following septum resection are shown in tables (1-2).

3. Results

Table (1): Reproductive outcome before and after monopolar hysteroscopic metroplasty.

Reproductive outcome			Before metroplasty ^(a)		After metroplasty ^(b)		P value
1.	One or two abortions	N%	3/20	(15%)	3/23	(13.04%)	0.179 (NS)
2.	Recurrent (habitual) abortions)	N%	8/20	(40%)	3/23	(13.04%)	0.022 (S)
3.	Preterm delivery(s)	N%	7/20	(35%)	2/23	(8.69%)	0.041 (S)
4.	Complications during pregnancy	N%	15/20	(75%)	5/23	(21.73%)	0.028 (S)
5.	Total pregnancy loss	N%	16/20	(80%)	5/23	(21.73%)	0.017 (S)
6.	Infertility ^c	N%	6/26	(23.07%)	3/26	(11.53%)	0.035 (S)

a. Total number 20 patients have achieved pregnancy before metroplasty

b. Total number 23 patients have achieved pregnancy after metroplasty

c. Out of 26 patients included in the study group.

Our study included 26 patients, the mean age of the patients was 29.73 ± 6.12 years (range, 24-35), mean parity was 1.15 ± 1.22 (1-2), 6 patients were nulligravida and 3. patients (.15%) had undergone spontaneous abortions (lor2 abortions) 8 patients

(40%) had Recurrent (habitual) abortions, 7 patients (35%) had preterm delivery, and 2 patients (10%) had a previous full term pregnancy with pregnancy complications.

Table (2): Pregnancy complication and mode of delivery before and after hysteroscopic metroplasty.

		Before metroplasty ^(a)		After metroplasty ^(b)		P value
1.	Bleeding in early pregnancy	7/20	(35%)	3/23	(13.04%)	0.039 (S)
2.	Antepartum hemorrhage	3/20	(15%)	3/23	(13.04%)	0.365 (NS)
-	Placenta previa	2/20	(10%)	2/23	(8.69%)	0.107 (NS)
-	Abruptio placenta	1/20	(5%)	1/23	(4.34%)	0.217 (NS)
3.	Preterm labor	7/20	(35%)	2/23	(8.69%)	0.032 (S)
4.	Premature rupture of membrane	3/20	(15%)	3/23	(13.04%)	0.641 (NS)
5.	Delivery ^c	9/20	(45%)	16/23	(69.56%)	0.022 (S)
-	NVD	4/20	(20%)	6/23	(26.08%)	0.117 (NS)
-	Instrumental	2/20	(10%)	3/23	(13.04%)	0.238 (NS)
-	CS	3/20	(15%)	7/23	(30.43%)	0.036 (S)

a. Total number 20 b. Total number 23 c. including preterm and full term delivery.

In our study, there were 5 cases with arcuate uterus, 4 cases with complete septum and single cervix, 2 cases with complete septum and double cervix, and 15 cases with sub septate uterus according to ASRM guidelines (16).

Obstetric outcome.

As regarding neonatal outcome, the number of full term deliver and the neonatal weight was significantly higher after hysteroscopic metroplasty {7/20 (35%) before metroplasty vs. 15/23 (62.21 %), and 2261.13 ± 2.14 g before metroplasty vs. 2850.77 ± 8.51 g, $P < 0.001$ j, with a significant increase in the mean gestational age at delivery after hysteroscopic metroplasty (31.21 ± 3.45 wks vs. 38.85 ± 7.65 wks before metroplasty ($P < 0.05$). Early neonatal condition judged by Apgar scores both in 1 and 5 min after delivery was significantly improved after hysteroscopic metroplasty {5/7 (71.42%) before

metroplasty vs. 3/15 (20%) after metroplasty) for low apgar score in 1 min and it was ! 5/7 (71.42%) before metroplasty vs. 1/15 (6.66%) after metroplasty) ($P < 0.001$). Consequently the admission to NICU was significantly lower after Hysteroscopic metroplasty !5/7 (71.42%) before metroplasty vs. 2/15(13.33%) after metroplasty, $P < 0.05$).

4. Discussion

In this retrospective study of 26 women we supported the use of hysteroscopic septum resection to improve pregnancy loss (86%) and infertility (32%).

Septate uterus is the most common (35%) with an incidence of 1-2% in the general population, while in women with repeated pregnancy loss it is significantly higher (3.3%) (1, 2).

Hysteroscopic metroplasty has outdated and replaced Tran abdominal metroplasty by enabling

vaginal approach to the correction of septate uterus and providing several advantages such as simple and short surgery with shorter hospitalization time, such factors make hysteroscopicmetroplasty a superior approach to abdominal metroplasty (9).

In our study, after metroplasty, there were impressive changes in the results, as 23 * patients, out of 26 (88.46%) became pregnant, 3 patients (13.04%) ended in one early abortion, 3/23(13.04%) had habitual abortion, 2 patients (4.34%) ended in preterm labor, 14/23 (60.86%) had reached to term delivery with a total pregnancy loss of 5/23 (21.73%) and pregnancy complication has in 5/23 (21.73%) and of these patients 13/23 (56.52%) living babies were recorded, and these results represent a statistically significant difference than before metroplasty (P<0.05).

Retrospective studies (1, 8, 11) have shown an improvement in the rate of live births following hysteroscopicmetroplasty, however, a controlled prospective study on women having malformed uteri and recurrent spontaneous abortions found no benefit to hysteroscopic surgery (12), while on the other hand some (4) reported that hysteroscopic septum resection in 25 patients was followed by lower rates of first-trimester and total pregnancy loss, as after correction. The total rate of spontaneous abortion fell from 93.2% to 40.4% and only 2 of 44 pregnancies resulted in the delivery of a viable neonate before metroplasty and 59.6% after the procedure—although only 44.2% of deliveries occurred at term.

Similarly, better pregnancy outcomes were noted by Grimbizis and coworkers (8) and Pabuc. cu and Gomel (1) after hysteroscopicmetroplasty in women with recurrent 'spontaneous abortion and septate uteri as in this study, and also, they reported spontaneous abortions rates about (11-25%) and rate of term delivery about (64-72%). Choe and Baggish (13), and Fedele and Vercellini (14) evaluate the effectiveness of hysteroscopicmetroplasty for the reproductive outcome of septate uterus suggested that this procedure decreased the miscarriage rate from 60% down to 15% and increased the pregnancy rate significantly from 5-20% to 81-91%, also, the results of Saygili Yilmaz et al. (9) were compatible with the results of this study as the total miscarriage rate dropped down to 16.1% from 94.3% and the total term pregnancy rate of our cases increased to 65% from 0.4%.

The results of this study and the data of other several studies confirm that the hysteroscopicmetroplasty should be considered as the most effective approach in women with septate uterus when there is a history of miscarriage, preterm labor or complicated pregnancy and support theories that consider the structural alteration of uterine septum and a different vascularization of the endometrium as the main reasons for the poor pregnancy outcomes, and

expect better pregnancy outcome in anomalous uteri without septa (15).

In our study, as regarding neonatal outcome, there was significant improvement in the neonatal weight, Apgar scores, and the mean gestational age at delivery, before and after hysteroscopicmetroplasty (P< 0.05). These results were proved also by many other retrospective and prospective studies (1,8), and this supported the theory of 'inadequate intrauterine nourishment' due to congenital alterations of the uterine vascularization, which may compromise uteroplacental blood flow, that may be the cause of intrauterine growth retardation seen in malformed uteri (17).

Also, in the author opinion, in addition to the improvement of the uterine anatomy and uterine reproductive physiology after metroplasty whatever the approach, there was improvement in the level of the obstetric care received by the patients as before' diagnosis (and spontaneous abortion), most women do not receive high-risk obstetric care and after one or more spontaneous abortions, they are more likely to receive high-level obstetric care.

Furthermore, after metroplasty, these pregnancies are managed by different physicians using different treatment protocols; therefore, it is difficult to ascribe a better pregnancy outcome after metroplasty solely to the operative procedure (18).

In our study, there was no significant difference between normal spontaneous and instrumental vaginal deliveries before and after metroplasty (P> 0.05), while paradoxically CS rate was significantly higher after hysteroscopicmetroplasty {2/20 (10%) before metroplasty vs. 7/23 (30.43%) after metroplasty, P< 0.001}, which was higher than in the general population and this can be explained by that although the patients were informed about the possibility of vaginal delivery.

The majority of them - especially the term group - preferred cesarean delivery not because of obstetrical indications but for the preciousness of the pregnancy due to their history of infertility and poor reproductive outcome. The significant improvement in the reproductive outcomes in the study group after hysteroscopicmetroplasty may be due to the difference between the path morphology and the ultra-structure between uterine septum and uterine wall, as the amount of the endometrial glands on septum was less than that on the uterine wall, also the positive index level of estrogen and progesterone receptors on the septum was weaker than that on the uterine wall, as well as the densities of the smooth muscle cells were thicker and the collagenous fibers were sparser in the base and the middle of the septum compared with uterine wall, with rare amount of small arteries in the septum (17). Also, in the study of uterine artery

Doppler velocimetry indices after metroplasty in arcuate uteri demonstrated that metroplasty, as well as making the uterine cavity wider, leads to better uterine perfusion, as uterine artery Doppler velocimetry (was studied transvaginally before and after metroplasty), was improved as assessed by lower mean pulsatility index (PI) (18).

So, the improvement in the path morphology and the ultra-structure of the uterine wall alter metroplasty will increase the reproductive prognostic index of patients with uterine septum.

In our study, 2nd look office hysteroscopy revealed 5 women (19.23%) with residual septum, 2nd film of hysterosalpingogram demonstrated that 3 patients (11.53%) of them with the septum <1 cm in thickness and need no intervention, and only 2 patients (7.69%) had a residual septum >1 cm and 2nd intervention using office hysteroscopy was done. These results were comparable to that of Litta et al. (19) using the same technique Fedele et al. (21) published that small residual septum (<1 cm) after hysteroscopic septum resection does not impair the reproductive outcome.

Kucera (10), calculated an index where the septum as well as the uterine cavity changes after resection, and the results showed a higher incidence of spontaneous abortions when the calculated ratio was >10% in our study, the efficacy and safety of the hysteroscopic procedure with a monopolar electrode system were assessed compared with a resectoscope technique.

The reproductive outcome rates after metroplasty were 77% using the resectoscope and • 74% with monopolar (19), and 60.86% full term deliveries in this study.

The operating time was significantly shorter {19.6 ± 4.32 min (range 13-35 min)}, in this study compared with the resectoscope procedures (1, 8).

In our study intrauterine adhesions were observed in 3 patients (11.53%) which were very thin and small, removed easily using office hysteroscopy Among the different instruments available for resection of the septum, 4 mm endoscopic scissors, the resectoscope, rigid micro scissors or lasers (18, 20), Recently used bipolar energy has been introduced, keeping the same outcome rate but with broad safety profile (19).

Current techniques of operative hysteroscopy used for treating septate or sub septate uterus use a monopolar electro-surgical system; the distension medium is usually sorbitol and glycine.

This limits the operative time in order to decrease the incidence of fluid overload, which may lead to reproductive outcomes after hysteroscopic metroplasty lead to hyponatraemia and subsequent cerebral edema and death. The normal saline used has ion concentrations similar to human plasma and may reduce electrolyte changes and hyponatraemia (21).

A second advantage of the monopolar system is that cervical dilatation is not required. Such dilatation is often difficult in nulliparous women with a stenotic cervix. Avoiding cervical dilatation should prove advantageous in reducing the risk of cervical laceration and uterine perforation and in postoperative analgesia requirements. A third potential advantage is that this monopolar system might prevent electro-surgical genital tract burns with excellent haemostasis was achieved in the vapourcut mode which is likely to be advantageous in infertility surgery (22).

The previous data and the results of this study, demonstrated that monopolar hysteroscopic metroplasty is a simple, prompt and less invasive procedure with minimal intraoperative and postoperative morbidity, with a shorter hospital stay, a reduced recuperation time, a decreased need for analgesia, a shorter interval before conception, a lower risk of uterine rupture during pregnancy, and the possibility of planning a vaginal delivery.

Conclusions

Hysteroscopic metroplasty using the monopolar is a successful alternative to the resectoscope technique; it has the same effectiveness and broad safety profile with its simplicity, minimal postoperative sequelae, and improved reproductive outcomes, this approach should be recommended for metroplasty.

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