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Effectiveness of Hysteroscopic Transcervical Resection of Uterine Septum (HTCRS) in Improvement of Reproductive Outcomes: Misurata Experience

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ABSTRACT

Objective: *To evaluate efficacy & safety of HTCRS in improvement of reproductive outcomes (RO) in women with history of infertility, recurrent miscarriages (RM) or preterm birth (PB).*

Patients and Methods: *Retrospective descriptive study of 210 patients of 24 to 42 years old, with primary or secondary infertility or with history of (RM) whom underwent HTCRS. Follow-up with (HSG) & hysteroscopy after 3 months, if necessary, surgery repeated. Pregnancy rate (PR), (RO)& complications within one year after surgery were evaluated.*

Results: *pregnancy achieved in 102/178 (57.3%). Patients ended in miscarriages; 12 (11.7%), 85 (83.3%) infants born at term, 5 (4.9%) born premature. No ectopic pregnancies. Miscarriage rates (MR) and (PB) reduced as compared to before surgery. NO major complications. No significant difference between age, BMI, infertility type & duration.*

Conclusions: *HTCRS is safe & effective in management of patients with infertility and (RM), increases (PR) & improving (RO) by reducing both (MR)&(PB).*

Keywords: *Uterine Septum, Infertility, Recurrent Miscarriages, Hysteroscopic Resection, Reproductive Outcomes.*

INTRODUCTION

Successful pregnancy outcomes depends on several factors, among which embryo qualities and intrauterine environment play major roles for the achievement and continuation of pregnancy (1). Small intrauterine lesions such as septum, adhesions, polyp, and submucous myoma are likely to be considered in causing implantation failure (2). A uterine septum is the most common congenital uterine anomaly with an incidence of 3%-4% in general female population (3,4), and to be significantly higher in patients with infertility and recurrent pregnancy loss (4,5). It results from incomplete resorption of the medial septum after complete fusion of the müllerian ducts has occurred. Numerous septal variations exist. The complete septum extends from the fundal area to the internal cervical orifice and divides the endometrial cavity into two components. This anomaly is often associated with a longitudinal vaginal septum.The partial septum does not extend to the internal cervical orifice(6).Uterine septum is associated with high rate of spontaneous miscarriages (21%-27%) and premature delivery (12-33%), as well as a low term pregnancy rate (40%-43%) (7-9). A septate uterus is also seen in about one-third of women with recurrent miscarriages who are diagnosed with Müllerian anomaly (10) In addition, septate uterus is associated with a high prevalence of both repeated assisted reproductive technology (ART) failure (18.2%) (11) and early pregnancy loss after ART (9.7%) (12). There are several ideas about the underlying mechanism of the implantation failure or pregnancy loss. Septum tissues have fewer blood vessels and a relatively high fiber content, and the endometrium covering the septum shows a relatively poor response to hormones, affecting fertilized egg

implantation as well as normal growth and development of the placenta, which may lead to infertility, miscarriage, premature birth, abnormal fetal position, and so on. (13,14).

The reproductive history of recurrent miscarriage or fetal loss is considered an important indication for uterine septum treatment (15-17). Alternatively, the issue of uterine septum and infertility remains controversial, with both limited and conflicting data in the literature (7,18-21) . Some reports suggested that HTCRS in patients with unexplained infertility increases natural and after ART conception rates as well as live birth rates, and decreases the risk of miscarriage (22-26).The incision of the septum can be carried out by resectosope, scissors, or laser, and none of these technique seem to have any apparent advantage over the others (16, 27-29). Most recently, it has been reported that surgical management of complete uterine/vaginal septum with duplication of the cervix using a plastic needle guide juxtaposed the hysteroscopic scissors aids in stabilization of septum during excision and facilitating safe take down and such approach might help to enhance efficacy and safety of uterine septal resection (30). However, advantages of HTCRS has been linked to shorter hospitalization time, a lower risk of pelvic adhesions, and reduced morbidity. The procedure also allow women to retain the option of subsequent vaginal delivery (31-33). The present study aims to evaluate the efficacy and safety in addition to the reproductive outcomes following HTCRS in a retrospective series of women with history of infertility or recurrent miscarriages.

PATIENTS AND METHODS

This retrospective descriptive study included 210 patients who underwent HTCRS from March 2012, through January 2015 at Misurata Teaching Centers. Patients age was ranging from 24 to 42 years: 146 with primary infertility, 50 with secondary infertility & 14 with histories of recurrent miscarriages (RM) (≥ 2 miscarriages). Written informed consent was obtained from all patients in order to use the data for future scientific research. The Ethics Committees concerned at those Centers approved this study. Septum diagnosis was made during the routine infertility work-up by hysterosalpingography (HSG) & hysteroscopy. Furthermore, laparoscopy was performed for differential diagnosis of septate and bicornuate uterus. Guidelines from the American Society for Reproductive Medicines or previously AFS (34) were applied for classification of the septate into the following two classes: i. Va (complete septate uterus) and ii. Vb (partial septate uterus). Three months after Hysteroscopic metroplasty, the patients with an indication for assisted reproductive technique (ART) including IUI and according to departmental protocols, underwent controlled ovarian hyperstimulation. After the surgery, patients were followed up for > 12 months for pregnancy status and outcomes.

Surgical Procedures

The HTCRS was performed in the early proliferative phase under general anesthesia. For complete septum, simultaneous laparoscopy was performed to rule out a bicornuate uterus. Resection procedures were performed with a 26 French resectoscope/ (Ackermann, Germany) with a cutting monopolar 90^0-angle knife electrode. The cutting current was set to 50-70 W. The uterine cavity was distended with 1.5% glycine at an inflow pressure of 70-100 mmHg. The inflow and outflow fluid volumes were measured to ensure that the differences never exceeded 1000ml. The resection began from the lower margin of the septum and continued with a progressive horizontal incision in the midline until both Ostia were equally visible on panoramic view. After division of the septum, uterine pressure was decreased and any bleeding points were cauterized. No intrauterine prosthetic devices were inserted postoperatively, butMoist Exposed Burn Ointment (MEBO) used in prevention of de novo intrauterine adhesions.There were 8 cases with vaginal septum, in which the septum was removed using Mets scissors (Aesculap Inc., Germany) followed by suturing then followed by HTCRS. To evaluate effectiveness of the procedure, follow-up diagnostic hysteroscopy was performed after three months, and if the result confirmed an inadequate resection, the residual tissue was removed in a second intervention.

Statistical Analysis

Data analysis was performed by means of SPSS version 13.0 software program (SPSS Inc., Chicago, IL, USA) through calculations of descriptive statistical methods (frequency, mean and standard deviation). McNemar's test was used to compare preoperative and postoperative outcomes. P value <0.05 was considered statistically significant.

RESULTS

The study included 210 patients, 146 (69.5%) patients were with primary infertility, 50 (23.8%) patients with secondary infertility, and 14 (6.6%) patients with RM. According to the results of HSG and diagnostic hysteroscopy of primary infertility patients: 136/146 (93.2%) had partial septum, whereas 10/146 (6.8%) patients had complete septum, while those of secondary infertility: 48/50 (96%) patients had partial septum, only 2 (4%) women were with complete septum. Patients of recurrent miscarriages: 12/14 (85.7%) were with partial septum, just 2/14(14.2%) had complete septum. (Table1). Mean age, body mass index (BMI), mean duration of infertility, and number of patients with histories of ART and IUI are shown in (Table 1). The septum was completely removed during the first time of hysteroscopic surgery in 198/210 (94.2%) patients. On post operative follow-up HSG or hysteroscopy, a residual septum was seen in 12/210 (5.7%) patients in whom the septum was completely removed in the second intervention. Two cases were complicated by small perforations, managed conservatively and did not need any additional intervention. Bleeding was encountered in one case and got controlled by a Foley catheter. There were no cases of postoperative Asherman's syndrome.

Table1. *Clinical Data of the Study Groups*

	Primary Infertility	**Secondary Infertility**	**RM**	**Total**
Patient	**146**	**50**	**14**	**210**
Type of septum Partial Complete	 136 (93.2%) 10 (6.8%)	 48 (96.0%) 2 (4.0)	 12 (85.8%) 2 (14.2%)	 196 (93.3%) 14 (6.6%)
Age	30.3±5.2	32.5±4.6	30.4±5.5	30.1±5.6
BMI (Kg/m2) (Mean ±SD)	27.5±4.5	27.4±3.2	28.3±3	
Infertility duration	7.6±5.2	9.3±6.5	-	7.95±5.5
Patient with history of ART	27 (18.4%)	8 (16.0%)	1 (7.1%)	36 (17.1%)
Patient with history of COH+IUI	12 (8.2%)	3 (6.0%)	2(14.2%)	17 (8.1%)

While 32 (15.2%) patients were lost in the follow-up period, only 178 out of 210 patients were available for outcome analysis: Pregnancy was achieved in 102/178 (57.3%) women: 58/102 (56.8%) naturally, 33/102 (32.3%) after ART and 11/102 (10.7%) after IUI. Among those patients, 12/102 (11.7%) pregnancies ended in miscarriages: 5 following ART, 2 after IUI, and 5 women who conceived spontaneously. Pregnancies ended with PB in 5/102 (4.9%) patients, and 85/102 (83.3%) resulted in term deliveries. Before septum resection there were 42/178(23.6%) miscarriages, 21/178 (11.8%) preterm birth, and 15/178 (8.4%) full term delivery. After HTCRS, miscarriage rate was significantly reduced to 12/178 (6.7%), ($P< 0.05$), preterm birth was also reduced to 5/178 (2.8%) and full term deliveries were significantly increased to 85/178 (47.7%).No ectopic pregnancies were recorded after septum resection. (Figure1).

Table2. *Pregnancy rate and outcome after HTCRS.($P< 0.05$)*

Parameter	**Primary Infertility**	**Secondary Infertility**	**RM**	**Total**
Patient	146	50	14	210
Lost in follow up	24 (16.4%)	6 (12.0%)	2 (14.3%)	32 (15.2%)
Tend to get pregnant	122 (83.6%)	44(88.0%)	12 (85.7%)	178 (84.8%)
Pregnant • Natural • After ART • After IUI	73 (50.0%) 35 (47.9%) 28 (38.3%) 8 (10.9)%	21 (42.0%) 17 (80.9%) 4 (19.0%) 2 (9.5%)	8 (57.1%) 6 (75.0%) 1 (12.5%) 1(12.5%)	102 (57.3%) 58 (56.8%) 33 (32.3%) 11 (10.7%)
Miscarriages	7 (9.5%)	5 (23.8%)	0	12 (11.7%)
Preterm birth	2 (2.7%)	3 (14.2%)	0	5 (4.9%)
Term delivery	64 (87.6%)	14(66.6%)	8 (100%)	85 (83.3%)

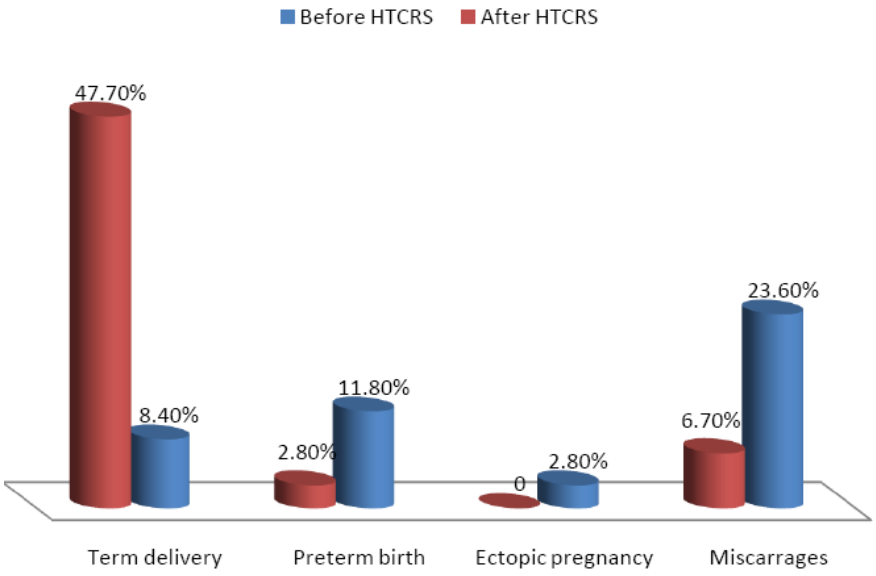

Figure1. *Pregnancy outcome before and after HTCRS.*

DISCUSSION

Septate uterus is considered to be the commonest congenital uterine malformation associated with very poor reproductive performance and high miscarriage and low term pregnancy rates if not treated. HTCRS is a safe and routinely used procedure for the treatment of septate uterus in patients with a history of repeated abortion, preterm birth, and infertility (1,20,23,26,35). However, there is controversy about whether to offer HTCRS to women with uterine septa, or wait until miscarriage occurs or pregnancy fails (36-38). Although there are no prospective randomized controlled trials, studies have shown that HTCRS helps increase the rate of pregnancy and live and term births and thus contributes to an improvement in obstetric outcomes (7,23, 26,35, 38- 42).

In our study, the overall pregnancy rate after HTCRS was 57.3% which was in the range of results of other studies (40%, 44%, 45.8%, 57.5%,60%) (30,35,39,41,43,44). After HTCRS, miscarriage rate was significantly decreased to 6.7%, ($P< 0.05$). The rate of preterm birth was also reduced to 2.8% , and term deliveries were significantly increased to 47.7%.Previous studies also showed decreased miscarriage rate (5-20%) and increased live birth babies (62-87%)(35,39,43,45). This reproductive outcome improvement following HTCRS might be related to an increased volume of uterine cavity, which create an appropriate location for implantation and enhanced endometrial function via re-vascularization of uterine connective tissue (46,47).Previous studies indicated that HTCRS is valuable in patients with recurrent miscarriages (17,48). In case of patients with infertility, although some studies showed improved pregnancy outcome among them after HTCRS (35,41,42), others have reported conflicting results (20,23,37). Moreover, retrospective studies showed comparable implantation and pregnancy rates in ART cycles for patients with septa and without septa (49). On the other hand, another retrospective, matched, controlled study, suggested that the presence of septate uterus might lead to decreased pregnancy rate and increased miscarriage rate after ART and both outcomes were improved after HTCRS (24). In our study, evaluation of the recurrent miscarriage group showed that 57.1% of those who tended to get pregnant conceived after HTCRS and all of them ended in term deliveries. In evaluating the infertile group, 47.9% of pregnancies in patients with primary infertility and 80.9% of pregnancies in those with secondary infertility were natural conception after HTCRS.The term delivery rate was also improved after HTCRS in patients with primary infertility: (87.6%) and (66.6%): in patients with secondary infertility. Such improvement was also concluded by previous studies (40,42,44,50)and that justify performing HTCRS in patients with infertility. Also among102 patients who had HTCRS and did not conceive naturally, 33 (32%) became pregnant after ART.

Different treatment protocols after HTCRS to prevent Asherman's syndrome have been studied. It was in form of hormone therapy (estrogen and progesterone) to stimulate endometrial growth, placement of intrauterine

device (IUD) or balloon to maintain the uterine cavity and prevent septal fusion. Some authors did not use hormonal therapy but concluded improved pregnancy rate (23,35,51). Other studies have also shown that neitherIUD or balloon placement, nor estrogen treatment, or both prevent intrauterine adhesions or facilitate pregnancy post HTCRS (52,53),while others showed improved pregnancy rate after hormonal the rapyor IUD or both.(41,55, 56). In our study, postoperatively, we did not use hormonal therapy or IUD, instead we used Moist Exposed Burn Ointment (MEBO) to prevent intrauterine adhesions. It is a safe herbal product containing phytosterols with anti-inflammatory, antibacterial in addition to analgesic effects, and significantly reduces the formation of de-novo intrauterine adhesions and it's severity (57). The complication rate was very low (1.5%), 2 cases of small perforation and one was bleeding which managed conservatively. In addition the prevalence of residual septum after first HTCRS in our study was (5.7%), lower than results reported by others (58,59).

CONCLUSION

The present study, showed that in women with septate uterus and a history of infertility or recurrent miscarriages, HTCRS is a safe and efficient procedure resulting in higher pregnancy rate, decreased miscarriage and increased full term delivery rates. However, more randomized controlled trials are needed, which could provide the highest level of evidence and substantiate the effectiveness of the HTCRS among infertile women.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Financial Disclosure

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Author Contributions

AME designed the study, data collection, conducted the clinical work and writing Manuscript**. FME**- conducted the Literature Search, statistical analyses/Interpretation, and critical review. All authors approved the final manuscript.

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