

Reproductive performance after hysteroscopic metroplasty in infertile women: complete versus partial uterine septum

B. Karadag¹, B. Dilbaz², B. Demir², I. Ozgurluk³, M. Kocak⁴, Y. Karasu¹, E. Gulsah Sahin⁵, S. Dilbaz⁶

¹ Ankara Teaching and Research Hospital, Department of Obstetrics and Gynecology, Ankara

² Etlik Zubeyde Hanim Women's Health Teaching and Research Hospital, Department of Obstetrics and Gynecology, Ankara

³ Kangal State Hospital, Department of Obstetrics and Gynecology, Sivas

⁴ Private Edremit Gulf Hospital, Department of Obstetrics and Gynecology, Balıkesir

⁵ TEB Erzurum Karayazı State Hospital, Department of Obstetrics and Gynecology, Erzurum

⁶ Düzce University, Faculty of Medicine Department of Obstetrics and Gynecology, Düzce (Turkey)

Summary

Objective: To investigate the impact of hysteroscopic metroplasty on pregnancy outcome in women with complete or incomplete uterine septum (US) accompanying infertility. **Materials and Methods:** Seventy-three patients who had hysteroscopic metroplasty for complete and incomplete US with primary and secondary infertility were reviewed. Obstetric outcomes (number of pregnancies, live births, and miscarriages) up to 36 months follow up period were investigated. **Results:** Twenty-five patients in complete US and 28 patients in incomplete US became pregnant in 36 months follow up. Postoperative miscarriage rate was significantly lower in patients with complete US ($p = 0.0001$, $p = 0.0001$, respectively). The mean gestational week at the time of birth and mean birth weight of the infants were significantly lower in patients with complete US compared to the incomplete US cases ($p = 0.026$, $p = 0.049$, respectively). Postoperative pregnancy rate was significantly lower in incomplete US patients with primary infertility compared with secondary infertility ($p = 0.037$). **Conclusion:** Hysteroscopic metroplasty improves fertility and pregnancy performance. This improvement is more prominent in patients with complete US, and incomplete US patients with secondary infertility.

Key words: Complete uterine septum; Incomplete uterine septum; Hysteroscopic metroplasty; Obstetric outcome.

Introduction

Uterine septum (US) is the most common uterine structural anomaly among the fertile population with a prevalence of 1-4.3%. Almost half of the (34-48%) uterine malformations are US [1-3]. During embryological development, fusion of the two paramesonephric Müllerian ducts forms the uterus. Unification of the uterine cavity begins during the first trimester of the embryonic life from the uterine cervix proceeding caudally towards the fundus. A failure of the reabsorption process of the midline septum causes US. The degree of septation is variable; complete septum extends from the uterine fundus to the cervix, while incomplete septum demonstrates resorption of a portion of the caudal aspect of the septum [4].

Hysteroscopic metroplasty (hysteroscopic resection of the US) reduces intra- and postoperative morbidity and accepted as the method of choice for correction complete and incomplete US. Shorter operation time and hospitalization period are other advantages of this operation [5].

The negative impact of US on fertility is an interesting but still debated issue. Grimbizis *et al.* reported that the US is not an infertility factor, although it may contribute to the delayed natural conception of patients with secondary infertility [6].

However, an improvement in the pregnancy rate was reported after the hysteroscopic metroplasty in women with US and otherwise unexplained infertility, by various authors [7-9].

Many studies have described an increase in the pregnancy and a decrease in the miscarriage rates after hysteroscopic metroplasty in patients with complete US. Some authors believe that incomplete US is a variant of normal anatomy and it no impact on reproductive outcome [10, 11]. On the other hand, some studies reported an increased incidence of miscarriage and of preterm birth rate in women with incomplete US [12-15].

The first aim of the present study was to investigate the impact of hysteroscopic metroplasty on fertility rate and pregnancy outcome in women with complete or incomplete US accompanying infertility. The second aim was to assess if there was a difference in the pregnancy outcome following the hysteroscopic metroplasty, considering primary and secondary infertility.

Materials and Methods

A total of 131 patients who were treated with a hysteroscopic metroplasty in the Infertility Clinic in Etlik Zübeyde Hanım Maternity and Teaching Hospital between January 2007 and De-

ember 2008 were reviewed. The Institute's ethics committee approved the study protocol.

For the selection of the primary or secondary infertile patients, inclusion criteria were accepted as follows: women's age < 35 years, no endocrine-metabolic disorders including diabetes, hypo-hyperthyroidism, hypopituitarism, hyperprolactinemia, hyperandrogenism, no other coexisting infertility factors including endometriosis, tubal occlusion, ovarian cyst, decreased ovarian reserve (FSH > 12), history of primary or secondary infertility, and partner's spermiogram analysis in normal range. A total of 58 patients were excluded from the study for the following reasons: the indication of the operation for the pregnancy loss (n=41), coexisting pathology as diagnosed on the laparoscopy including endometriosis (n=8), tubal occlusion (n=5), and coexisting male factor infertility (n= 12). Eight couples had more than one cause of the infertility. Primary infertility was defined as the inability to conceive after one year of regular unprotected intercourse while secondary infertility was defined as the inability to get pregnant after 12 months of contraception-free intercourse after at least one pregnancy.

The initial diagnosis of US was made with hysterosalpingography (HSG) and confirmed by laparoscopy carried out simultaneously with hysteroscopic metroplasty. US was classified according to the American Society of Reproductive Medicine (ASRM) classification. US was categorized as type a (complete) or type b (incomplete) [16]. Normal sperm parameters according to WHO criteria for sperm analysis were used for evaluation (a sperm concentration of $\geq 20 \times 10^6$, $\geq 50\%$ motility and $\geq 30\%$ normal morphology, $\geq 75\%$ viability with $\leq 1 \times 10^6$ white blood cells).

The operations were performed under general anesthesia in the proliferative phase of the cycle. Hysteroscopic metroplasty was performed using a monopolar cutting knife electrode with laparoscopic supervision (ten-mm fiberoptic resectoscope). The uterine cavity was distended with a 1.5% glycine solution. Continuous irrigating flow with Hamoumat was used. Complete US was incised from the internal orifice of the cervical canal, up to the base of the septum until both of the tubal ostia were visualized at the same level. Tubal patency was tested during the laparoscopic observation. Intrauterine device was not inserted after the procedures. Postoperative diagnostic hysteroscopy and/or HSG were used asses the uterine cavity two to three months after surgery in all patients.

Follow-up after the hysteroscopy was done either in the infertility outpatient clinic or by phone with the form that contained the following data: number of pregnancies achieved, time interval between hysteroscopic metroplasty and pregnancy, number of miscarriages, ectopic pregnancies, and live births, gestational week at birth, and birth weight of the infant. The reproductive performance, time to achieve pregnancy, pregnancy rate, and obstetric outcome of the patients with complete and incomplete US in patients with primary or secondary infertility were compared.

The Statistical Package for Social Sciences (version 17.0) was used for analysis. Kolmogorow-Smirnov was used to test distribution of the continuous variables. Student *t*-test was used for variables with normal distribution. After testing the skewed distribution, comparisons between the groups were tested using the Mann-Whitney U test. The χ^2 test and Fisher's exact test were used to analyze nominal variables. McNemar test was used comparing the pre-post operative miscarriage rates. Continuous variables were expressed as mean \pm SD. $P < 0.05$ was considered as statistically significant.

Results

Overall 73 infertile patients with complete (n=32, 43.8%) and incomplete (n=41, 56.2%) US were evaluated. Twenty-

Table 1. — *The main characteristics and obstetric history of complete and incomplete septum groups before hysteroscopic metroplasty.*

	Complete uterine septum (n=32)	Incomplete uterine septum (n=41)	<i>p</i> value
Age (years)	25.1 \pm 4.7	27 \pm 5.2	NS
Primary infertility	14 (43.8)	13 (31.7)	NS
Secondary infertility	18 (56.2)	28 (68.3)	NS
Live birth rate (%)	2.2	17.3	0.035
Miscarriage rate (%)	86	71.7	NS
Duration of infertility (months)	35.3 \pm 26.3	43.4 \pm 35.8	NS

NS: non-significant.

Table 2. — *Pregnancy rate and pregnancy outcomes after hysteroscopic metroplasty.*

	Complete uterine septum (n=32)	Incomplete uterine septum (n=41)	<i>p</i> value
Pregnancy rate (%)	78.1	75.6	NS
Miscarriage rate (%)	3.1	26.3	0.035
Mean gestational weeks	36.4 \pm 5.1	39.1 \pm 1.1	0.026
Mean birth weight (g)	2733 \pm 994	3202 \pm 405	0.049
Live birth rate (%)	68.7	65.8	NS

NS: non-significant.

seven of these women (37%) had primary infertility while 46 (63%) had secondary infertility. The mean age of the patients was 26.2 ± 5 years and the mean duration of infertility was 39.9 ± 32 months. Live birth rate was significantly higher in patients with US before hysteroscopic metroplasty (19.5% vs. 3.1%, $p = 0.035$). The main characteristics and obstetric history of the patients before hysteroscopic metroplasty are presented in Table 1. The range of the patients' follow up period was 24 to 36 months.

After the procedure, two cervical lacerations on the tenaculum application site were observed; one of them required suture. Postoperative evaluation of the patients revealed normal shaped cavity in all patients.

Pregnancy rates were similar in both complete and incomplete US groups. Twenty-five patients in complete US and 28 patients in incomplete US became pregnant in 36 month follow up period. A total of 32 pregnancies was observed in complete US and 38 in incomplete US. Miscarriage rate and live birth rate calculated from total pregnancies. There was a significant decrease in postoperative miscarriage rates in both complete and incomplete US patients after operations in comparison to preoperative period ($p = 0.0001$, $p = 0.0001$, respectively). The decrease in miscarriage rate was more prominent in patients with complete US than incomplete US ($p = 0.035$). The mean gestational week at the time of birth and mean birth weight of the infants were significantly lower in patients with complete US compared to the incomplete US cases ($p = 0.026$, $p =$

Table 3. — Pregnancy rate and pregnancy outcomes after hysteroscopic metroplasty.

	Primary infertile patients (n=27)	Secondary infertile patients (n=46)	p value
Pregnancy rate (%)	62.6	84.5	0.037
Miscarriage rate (%)	7.7	14.9	NS
Mean gestational weeks	36.3 ± 4.5	38.7 ± 1.5	NS
Mean birth weight (g)	2720 ± 874	3116 ± 418	NS
Live birth rate (%)	92.3	91.5	NS

NS: non-significant.

0.049, respectively (Table 2). There was no difference in terms of the type of delivery (vaginal or cesarean section) between complete and incomplete septum groups ($p = 0.606$).

The pregnancy outcomes of the 73 patients with US were compared according to the type of infertility (primary and secondary infertility). Postoperative pregnancy rate was significantly lower in patients with primary infertility compared to the secondary infertility ($p = 0.037$). There was no significant difference in the miscarriage rate, live birth rate, mean birth weight, and mean gestational weeks at the time of birth between the patients with primary and secondary infertility (Table 3). The postoperative pregnancy rate was significantly lower in incomplete US patients with primary infertility compared to secondary infertility. (primary: 53.8%, secondary: 85.7%, $p = 0.037$).

Discussion

US is associated with poor pregnancy outcomes with an increased miscarriage and preterm birth rate. The negative impact of US on fertility is an interesting but still debatable issue. The presented data revealed that the reproductive performance of the patients with US was improved after the hysteroscopic metroplasty. However, observed improvements on the miscarriage rates were in favor of patients with complete US. Although no significant difference was observed on the live birth rate, the mean gestational week at the time of birth and mean birth weight of the infant were significantly lower in patients with complete US. Postoperative pregnancy rate was significantly lower in patients with primary infertility compared to the secondary infertility. Of interest, the postoperative pregnancy rate was significantly lower in incomplete US patients with primary infertility compared with secondary infertility. These results suggest that hysteroscopic metroplasty has a more beneficial effect on the achievement of pregnancy in secondary infertility.

Grimbizis *et al.* reported the incidence of miscarriage in patients with untreated US as 44% [3]. In another study assessing the reproductive outcomes with untreated complete septate uteri demonstrated a miscarriage rate of 27% [17]. Hysteroscopic resection of the septum improved the miscarriage rates in the range from 2.5% to 25% [3, 7, 8, 18]. In

the presented study, the miscarriage rates decreased significantly after hysteroscopic metroplasty in complete septum group (from 53% to 3.1%) and incomplete septum (from 61% to 19.5%) group. The decrease in miscarriage rate is more distinct in the complete US group. It can be speculated that the miscarriages observed in incomplete uterine cases might also be related to the other factors.

Abnormal uterine cavity, different structure of the septum, and dysfunction of the covering endometrium are thought to impair the reproductive outcomes in patients with US. In 1995, Fedele *et al.* reported that septum is a fibro-elastic tissue [19]. On the contrary, Dabirashrafi *et al.* noted that the muscular tissue was more than a connective tissue in the septum structure [20]. The altered proportion of the connective and muscular tissue in the septum may lead abnormal uterine contractility in the uterus. In the study presented by Fedele *et al.*, the maturation defect of the covering endometrium in the US was related to the infertility [21]. Recently, Raga *et al.* reported that the mRNA expression of the VEGF receptors was significantly lower on the covering endometrium of the septum. Authors suggest that local defect of VEGF receptors may lead to the poor vascular placentation that caused the poor reproductive outcome in pregnancies implanting the septum [22]. Restoration of the uterine cavity using hysteroscopy is intended to restore normal-adequate uterine cavity and uterine function, especially endometrium. In the present results, significantly lower gestational week at birth and mean birth weight of the infant may indicate that uterine volume in the complete US patients after hysteroscopic metroplasty, might be smaller than incomplete US patients.

Efficacy of prophylactic hysteroscopic metroplasty is controversial in infertile women without a history of adverse pregnancy outcome. Pregnancy rates in the literature after hysteroscopic metroplasty range from 38.6% to 81% in cases with infertility however a meta-analysis comparing the improvement in incomplete septum cases with complete septum cases is still lacking [8, 23]. Some studies failed to show a relationship between septate uterus and infertility as a considerable extent of women conceived without resection of the US [3, 4, 24, 25]. However, an improvement of the pregnancy rate was reported after the hysteroscopic metroplasty in women with US and otherwise unexplained infertility, by various authors [7-9].

Grimbizis *et al.* evaluated 42 US patients with infertility (primary: 26, secondary: 14). Following the hysteroscopic metroplasty, the pregnancy rates were 57.9% and 71.4% in patients with primary and secondary infertility, respectively. Postoperatively, 78.8% of the patients were treated by assisted reproductive technology (ART). Although statistical comparisons were not given, spontaneous pregnancy rate was lower in patients with primary infertility compared to the secondary infertility (15.8% and 35.7%, respectively). The pregnancy rate after ART was 42.1% for primary infertility and 35.7% for secondary infertility [6].

Pabuccu *et al.* investigated the reproductive performance after hysteroscopic metroplasty in patients with unexplained infertility. The pregnancy rate was given as 75% and 30.1% in patients with complete and incomplete US, respectively [7].

Mollo *et al.* investigated the impact of hysteroscopic metroplasty on the pregnancy rate in women with US and unexplained infertility. On the 12 months follow-up period, the pregnancy rate was 38.6% in women with US and unexplained infertility while 20.4% in the control group including unexplained infertile patients ($p < 0.05$) [8].

The retrospective nature and lack of control group are two potentially limitations of the presented study. However, observational management of women with US and otherwise unexplained infertility as control group would not be acceptable due to ethical difficulties. The valuable aspects of the presented study are long term follow-up period without additional treatment of the couples and comparing the data of reproductive outcomes in infertile couples with complete versus incomplete US.

In conclusion, hysteroscopic metroplasty improves the pregnancy rates and pregnancy outcome in the patients with US. This improvement is more prominent in cases with complete US, and incomplete US patients with secondary infertility. However, interference of US on women's fertility and improving effect on the infertility of hysteroscopic metroplasty in patients with unexplained infertility is still open to research and further analysis with larger series of patients is required.

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Address reprint requests to:

B. KARADAG, M.D.

Ankara Teaching and Research Hospital
Department of Obstetrics and Gynecology
Ulucanlar Street, 89
Ankara (Turkey)
e-mail: drburakkaradag@gmail.com