

Reproductive Outcome After Hystroscopic Metroplasty for Septate Uterus: Systematic Review

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Abstract:

Background: Still the effectiveness and safety of hystroscopic metroplasty in managing septate uterus is questionable as the current evidence of whether it improves reproductive outcomes is inconsistent.

Objective: To summarize the reproductive outcomes after hystroscopic metroplasty in women with septate uterus as well as to investigate whether pregnancy was normal or after in-vitro fertilization among those women.

Material and methods: A systematic review has been implemented according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) utilizing PubMed-MEDLINE, EMBASE, Google Scholar, Web of Science, The Cochrane Library and the Gynaecology and Fertility (CGF) Specialized Register of Controlled Trials electronic databases. Eligible studies were those including women diagnosed with either complete or partial septate uterus and managed by hystroscopic metroplasty versus no or other interventions (control subjects).

Results: A the final step, 12 studies with 1471 women diagnosed with septate uterus (partial/complete) were included in the present review. Miscarriage was reduced after hystroscopic metroplasty according to several studies while no significant differences were observed as regards the terms of live births and preterm labour between patients with hystroscopic metroplasty and those who had no intervention as indicated by some studies.

Conclusion: Hystroscopic metroplasty is of beneficial effect in reducing the risk of miscarriage and increase the rate of conception in women with septate uterus. However, larger, prospective trials before further made clinical decisions regarding the value of hystroscopic septum resection are recommended.

Keywords: Septate uterus, hystroscopic metroplasty, reproductive outcomes, Miscarriage, Live birth rate

Introduction

Septate uterus is a congenital anomaly resulted from resorption defect of Müllerian ducts, where the uterus is divided into two parts by a membrane called the septum which can vary in length and thickness and can extend to cervix and occasionally to the vagina.¹ It is a rare condition; however, it represents one of the more common uterine anomalies encountered in clinical practice representing 35-90% of congenital uterine anomalies.²

Septate uterus is associated with various adverse reproductive outcomes including infertility, recurrent loss of pregnancy loss, recurrent pelvic pain and preterm delivery.³

Diagnosis and management of septate uterus represents a challenge for gynecologists as a result of its multiple definitions and in addition, several cases are asymptomatic.^{4, 5} however, the standard management intervention for symptomatic cases is hystroscopic septal resection (Hystroscopic metroplasty).⁶

Up till now, effectiveness and safety of hystroscopic metroplasty is questionable as a method to manage septate uterus as the current evidence of whether hystroscopic metroplasty improves reproductive outcomes is inconsistent.⁷ A recent systematic review and metaanalysis study revealed that compared with untreated women, hystroscopic septum resection was associated with a lower rate of miscarriage with no significant impact was observed on rates of live birth, clinical pregnancy rate or preterm birth.⁶

As inconclusive evidence exists regarding the association between hystroscopic septum resection for women with septate uterus and previous poor reproductive outcomes, this review aims to summarize the reproductive outcomes (live birth, miscarriage, clinical pregnancy rate or preterm birth) after hystroscopic metroplasty in women with septate uterus as well as to investigate whether pregnancy was normal or after in-vitro fertilization among those women.

Materials and methods

A systematic review has been implemented according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).⁸

A comprehensive search was performed utilizing PubMed-MEDLINE, EMBASE, Google Scholar, Web of Science, The Cochrane Library and the Gynaecology and Fertility (CGF) Specialized Register of Controlled Trials electronic databases. The search was limited to studies published between 2000 and 2024 and English written. Hand search was also done for cross references from review articles and primary studies. Duplicates were identified and excluded.

The relevant keywords such as 'hystroscopic metroplasty' or 'septal resection' or 'hystroscopy procedure' or 'hystroscopy' and 'uterine septum' or 'septate uterus', or 'uterine anomalies' or 'uterine malformation' and 'reproductive outcomes' or 'live birth' and/or 'miscarriage', and/or 'clinical pregnancy rate' and/or 'preterm birth' and/or 'cesarean section/delivery' were utilized for searching.

Either prospective or retrospective cohort and case-controlled studies as well as randomized control trials comparing reproductive outcome (pregnancy, miscarriage, and live birth rates) between women with hystroscopic metroplasty for septate uterus and women without intervention before trials of pregnancy were included.

Eligible studies were those including women diagnosed with either complete or partial septate uterus and managed by hystroscopic metroplasty versus no or other interventions (control subjects). Studies with insufficient data regarding the reproductive outcomes have been excluded.

Screening for articles by titles and abstracts was implemented independently by the two authors to identify those fulfilling the inclusion criteria. Then, full texts of these articles were retrieved and assessed independently assessed by external two consultants in Obstetrics and Gynecology. Relevant data were extracted from these articles and tabulated in a specific sheet by the main author. Checking for accuracy of the included articles was discussed between the authors and the two obstetrics and gynecology consultants and the summary was presented in the PRISMA flow chart. Figure 1. The extracted data included: main author, year of publication, country of study setting, study design, number of study population, indicators of reproductive outcomes, main results and study limitations. Risk of bias in the included articles was independently checked by another two Obstetrics and Gynecology consultants utilizing the specific Newcastle-Ottawa Scale for cohort studies or case-control studies,⁹ and score of over 6 out of 8 was considered as low risk of bias.

Results

A total of 1028 studies were identified through the electronic research. Duplicates were removed both manually and by using Zotero Standalone software. Thus, a total of 629 studies were screened by titles and abstracts and 61 studies were evaluated for eligibility for inclusion.

At the final step, 12 studies with 1471 women with septate uterus (partial/complete) were included in the present review. As regards study design, 9 studies were retrospective^{10-16, 18, 21} while three studies were prospective.^{17, 19, 20}

With the exception of one study,¹¹ all included studies did not differentiate between partial and complete uterine septum.

Some important characteristics of the included studies are presented in Table 1, including year of publication, setting and design of the study, number of the participant, tools used to indicate reproductive outcomes, main results as well as study's limitations. According to the Newcastle-Ottawa Scale used for observational studies, none of the included studies were considered at high risk of bias. Miscarriage was reduced according to studies conducted by Omoto et al (2023),¹⁰ Hui-xiao et al (2021),¹¹ Chen et al (2013),¹⁵ Dalal et al (2012),¹⁶ Paradisi et al (2011),¹⁸ and Pai et al (2009).¹⁹

No significant differences were observed as regards the terms of live births and preterm labour between patients with hysteroscopic metroplasty and those who had no intervention as indicated by Hui-xiao et al (2021),¹¹ Chen et al (2013),¹⁵ and Pai et al (2009).¹⁹ However, higher rate of cesarean delivery was observed by Fox et al (2019),¹⁴ and Pabuçcu and Gome (2004).²⁰ One study reported data on fetal malpresentation. Rikken et al (2020)¹⁴ reported that foetal malpresentation occurred in 19.1% women who underwent septum resection versus 34.6% of women who had expectant management.

Table 1: Summary of the articles investigated the reproductive outcome of hysteroscopic metroplasty among women with septate uterus (2000-2023)

Author/s; year, country	Study design	Number of patients	Indicators of reproductive outcome	Main results	Main study limitations
Omoto et al, ¹⁰ 2023, Japan	A single-center retrospective study	27	The conception ratio (the number of women who achieved ≥ 1 conception/total number of women), the pregnancy loss ratio (the number of women who experienced ≥ 1 pregnancy loss/the number of women who conceived) and the take home baby (THB) ratio (the number of women who achieved ≥ 1 THB/total number of women)	Both abdominal and hysteroscopic metroplasty increased the THB rate by decreasing pregnancy loss without impacting the pregnancy rate.	-Being a single- center study. -Performance of the surgery by a solo surgeon -Small sample size. -Lacking of a control group
Hui-xiao et al, ¹¹ 2021, China	Retrospective cohort study	278 (87 with complete and 191 with partial septate uterus)	The miscarriage rate, the live birth rate and obstetric and neonatal outcomes	The miscarriage rate in women who underwent hysteroscopic septum resection, was significantly reduced from 5.1% to 12.9%. However, no significant difference as regards live birth rate, neonatal and obstetric outcomes between those who underwent hysteroscopic septum resection and their counterparts	-Being a single center study -Retrospective nature of its design
Rikken et al, ¹² 2020, The Netherlands, United States of America (USA) and United Kingdom (UK)	A multicentre retrospective cohort study	257	Rate of live birth, rate of ongoing pregnancy, pregnancy loss rate, preterm birth, and foetal malpresentation	Rate of live birth was 53% in women following a septum resection compared to 71.7% following expectant management and ongoing pregnancy occurred in 58.9% of women who underwent septum resection (58.9%), compared to 75.5% of those who had expectant management. Pregnancy loss occurred in 46.8% of women who underwent septum resection versus 34.4% of women who had expectant management while preterm birth occurred in 29.2% of women who underwent septum resection versus 16.7% of women who had expectant management while foetal malpresentation occurred in 19.1% women who underwent septum resection versus 34.6% of women who had expectant management	In this study, 19 of women who chose expectant management got pregnant at time of septate uterus diagnosis, compared to none of those who underwent septum resection.that could bias the findings. -The concepts of the classification of uterine anomalies particularly the differentiation between septate, arcuate and bicornuate uterus changed after collection of data. -The retrospective design of the study that depend on the quality of surgical care and accurate reporting.
Wang et al, ¹³ 2019, China	A single-center retrospective study	121	Term delivery rate, abortion rate, and the infertility rate	No serious post-hysteroscopic complications. However, uterine septa were reported in 4 cases after hysteroscopic metroplasty and 6 cases of intrauterine adhesions were reported after long-term follow-up. Term delivery rate has been increased while abortion rate has been decreased significantly in the three groups (complete uterine septum, women with uterine septum >2.5 cm, and women with uterine septum ≤ 2.5 cm) after surgery. The infertility rate was significantly lowest in group of women with uterine septum ≤ 2.5 cm after hysteroscopic metroplasty while the recurrent abortion rate was significantly lowest in group of women with complete uterine septum before surgery. After surgery, the infertility rate was significantly higher in group of women with complete uterine septum than in group of women with uterine septum >2.5 cm (28.6% vs. 10.5%). After at least 12-months of follow-up, the pregnancy rate in group of women with complete uterine septum was significantly lower than that in group women with uterine septum ≤ 2.5 cm (71.4% vs. 89.5%)	-The retrospective design -Absence of a control group -Relatively small sample size.
Fox et al, ¹⁴ 2019, USA	Retrospective cohort study	109 women (163 pregnancies)	Conception rate, cesarean section delivery rate	Higher rate of cesarean delivery was observed in the resected septum group compared to group with unresected septum. In nulliparous women, septum resection was associated with later gestational ages at delivery, decreased preterm birth <37 weeks gestation and an increased incidence of cesarean delivery in women who attempted vaginal delivery.	-Retrospective design -Relative small sample size
Chen et al; ¹⁵ 2013, China	A retrospective study	21	Pregnancy rate, spontaneous miscarriage and infertility	Pregnancy rate in the group with a poor reproductive outcome (spontaneous miscarriage or infertility) and underwent hysteroscopic metroplasty and removal of vaginal septum with the preservation of cervical septum was 81.8%. Of women who conceived, 66% had term delivery while in the group	-Small sample size -Retrospective design of the study -Being a single center study

				without a history of spontaneous miscarriage and did not undergo hysteroscopic transection of the uterine septum, 60% accepted surgery, and 50% had term delivery	
Dalal et al, ¹⁶ 2012 India	Retrospective study	72	Rate of coception -Rate of spontaneous abortion	Rate of coception was 45.8% within one year of hysteroscopic metroplasty with only 12% experienced spontaneous abortion and 15% had preterm delivery	-Small sample size -Single center -Retrospective design -No control group
Shokeir et al, ¹⁷ 2012 Egypt	A prospective study	144	Cumulative pregnancy rate, 24-month cumulative pregnancy rate	-Cumulative pregnancy rate was 51% after a mean follow-up of 41 months, with an overall 24-month cumulative pregnancy rate of 65%. -The 24-month cumulative pregnancy rate was 85% in women aged below 30 years, 66% in those aged between 30 and 35 years and 47% among those aged over 35 years. -The pregnancy rate in women with other minor infertility factors in addition to uterine septa was 55% while among those without such factors, it was 72%. -Pregnancy rate in women with less than 2 years versus 2 years or more of infertility were 85% and 50%, respectively	-Lack of a control group -Relatively small sample size.
Paradisi et al, ¹⁸ 2011 Italy	Retrospective study. They classified women into two groups; Group 1 (n= 108 women with unexplained infertility, and group 2 (n=138 women had recurrent abortion).	246	Pregnancy rate and miscarriage rate	In group 1, 56.5% of women had pregnancy; 19.7% of pregnancies ended in miscarriage. In group 2, 65.3% women had pregnancy; 34.1% of pregnancies ended in miscarriage.	-Single center -Retrospective design
Pai et al, ¹⁹ 2009 India	Prospective study	72	Conception rate, spontaneous abortion rate and preterm rate	33 women (45.8%) conceived within one year of surgery and 4 women (12%) had spontaneous abortions and 5 (15%) had preterm delivery; which indicate an overall improvement in reproductive performance of those women after hysteroscopic metroplasty	-Relatively small sample size -Absence of control group
Pabuçcu and Gomel, ²⁰ 2004 Turkey	Prospective study	61	Rate of conception	Rate of conception was 41% within 8–14 months after the procedure. Of them, 29.5% had live births and 11.5% experienced spontaneous abortions. Two-thirds of the women who had live births were delivered by cesarean section	-Small sample size -Single center -No control group
Porcu et al, ²¹ 2000 France	Retrospective study	63	Rate of pregnancy, rate of live birth,	Satisfactory outcomes were reported in 57.1% of cases. Rate of pregnancy was 71.4% (45 women); two after an in-vitro fertilization (IVF) program. Rate of live birth was 62.2% (n=28); majority of them (n=26) were born at term. Twenty patients delivered normally and two women were still pregnant at the time of study. Overall, obstetrical prognosis was improved by the treatment.	-Small ample size -Single center -Retrospective nature -Lack of control group

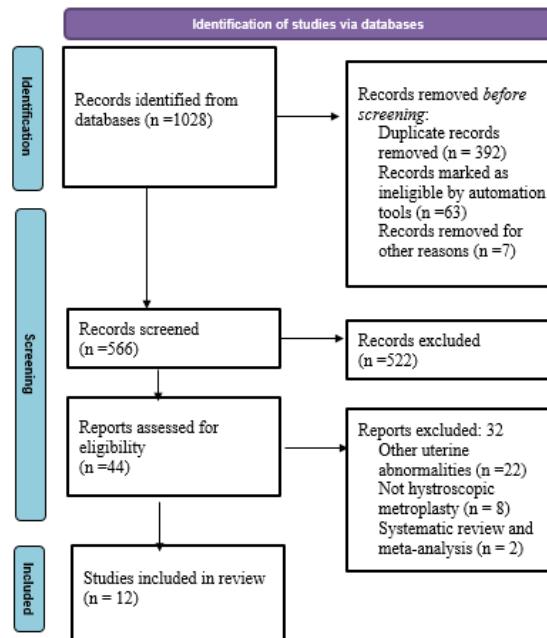


Figure 1: Flow chart of data extraction

Discussion

This systematic review offers up-to date information of the published studies investigating the highly controversial issue of the reproductive outcome of hysteroscopic resection of the uterine septum in women with septate uterus.

Overall, this review provides an evidence of the reduction in the risk of miscarriage following hysteroscopic metroplasty in women with uterine septate uterus (partial or complete). The same has been reported in relatively recent systematic reviews done by Carrera et al (2022)²² and Krishnan et al (2021).⁶ However, in this review we did not differentiate between partial and complete uterine septum. Carrera et al (2022)²² reported that the reduction in the risk of miscarriage was higher in women with complete setum, which supports the impact of a dose-response

gradient on the influence of hysteroscopic metroplasty on the reproductive outcomes. Additionally, the present review in accordance with Carrera et al (2022)²² suggested the beneficial effect of hysteroscopic metroplasty among women with septate uterus on reducing the rates of preterm birth and fetal malpresentation. However, Krishnan et al (2021)⁶ did not observe any significance suggesting that hysteroscopic resection improved live birth and clinical pregnancy rates, and/or decrease preterm labour. The actual mechanism through which a uterine septum is linked to adverse reproductive outcomes including miscarriage and preterm births is still not clear. However, many hypotheses have been suggested including insufficient vascularization of the septum and morpho-functional differences of the endometrium covering the septum.²² Additionally, Rikken et al (2019),⁴ indicated that the intrauterine septum consists of endometrium and myometrium close to those of the uterine wall. However, heterogeneity of the included studies limits the power of the evidence. This limitation in the available knowledge regarding the causal hypothesis for the reproductive outcomes attributable to uterine septum after hysteroscopic metroplasty necessitates stronger evidence on the usefulness of this managing procedure. Some important limitations should be addressed in this systematic review. First, majority of studies has small sample size and retrospective in nature as well as did not adjust their findings for confounding factors. Second, due to rarity of studies, in this review eligible studies were carried out across a long span (2000-2023) and during such long time, dramatic changes have been made in system classifications as well as surgical procedures. Third, heterogeneity of studies was clear as regards criteria for inclusion, outcome measures and duration of the follow-up period. Finally, most of the included studies did not account for the uterine septum size, which could impact the choice of treatment as well as the reproductive outcomes. Despite of those limitations, this review posse some strengths including the fact that a comprehensive strategy was used for literature review, and meticulous selection of the studies included in the final review was followed through a systematized scale and the final decisions on inclusion were made via broad consensus of experts. Furthermore, this systematic review could be of importance for clinicians in their decision regarding considering hysteroscopic resection of the uterine septum in women with previous history of infertility and/or adverse reproductive outcomes to decrease rate of miscarriage and malpresentation in labour.

Conclusion

The results of the present systematic review support the evidence that hysteroscopic metroplasty is of beneficial effect in reducing the risk of miscarriage and increase the rate of conception in women with septate uterus. However, due to methodological heterogeneity of studies and according to the findings of the present study in the absence of well-designed randomized studies, we can recommend hysteroscopic metroplasty in women diagnosed with a septate uterus. Furthermore, there is a need for larger, prospective trials before further made clinical decisions regarding the value of hysteroscopic septum resection.

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