

## Systematic Review and Meta-Analysis: Impact of Arcuate and Septate Uteri on Reproductive Failure in Spontaneous and IVF Cycles

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**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Risk of bias assessment.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202530071**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 March 2025 and was last updated on 16 March 2025.**INTRODUCTION**

**Review question / Objective** • Evaluating the impact of septate and arcuate uteri on implantation failure and live birth rates in spontaneous and IVF pregnancies.

- Examining whether the presence of fibrotic septal tissue alters decidualization and trophoblast function, thereby compromising embryo survival.
- Assessing the efficacy of surgical intervention (hysteroscopic metroplasty) in improving reproductive outcomes.

**Rationale** Rationale Despite the clear evidence of reproductive impairment in septate uteri, there remains uncertainty regarding the clinical significance of arcuate uteri. The distinction between these anomalies is clinically significant, as septate uteri are often treated surgically, whereas arcuate uteri are typically managed conservatively. Despite numerous studies, the precise impact of these anomalies on implantation failure and live birth rates remains controversial.

**Condition being studied** • Evaluating the impact of septate and arcuate uteri on implantation failure and live birth rates in spontaneous and IVF pregnancies.

- Examining whether the presence of fibrotic septal tissue alters decidualization and trophoblast function, thereby compromising embryo survival.
- Assessing the efficacy of surgical.

**METHODS**

**Search strategy** Search Strategy and Eligibility Criteria A comprehensive literature search was conducted in PubMed, Embase, CINAHL Complete, MEDLINE, PsycInfo, Global Health, Cochrane Library, Scopus, and UpToDate from 1980 to March 2025. The search terms included "uterine septum," "septate uterus," "arcuate uterus," "infertility," "implantation failure," and "sterility."

**Participant or population** Inclusion criteria encompassed randomized controlled trials (RCTs), prospective non-randomized studies,

observational studies, retrospective studies, and systematic reviews with meta-analyses, including Cochrane reviews. Studies were included if they reported on reproductive outcomes in women with arcuate or septate uteri, specifically addressing implantation failure and live birth rates in both spontaneous and IVF cycles. The PRISMA flow diagram illustrates the study selection process.

**Intervention** We conduct a Comprehensive Literature Search by using Boolean operators and / or to combine keywords ("uterine septum" OR "septate uterus" OR "arcuate uterus") AND ("infertility" OR "implantation failure" OR "sterility") AND ("RCT" OR "prospective" OR "observational" OR "retrospective" OR "systematic review" OR "meta-analysis") and by adjusting based on database-specific syntax. We performed Searches on Multiple Databases : PubMed, Embase, CINAHL Complete, MEDLINE, PsycInfo, Global Health, Cochrane Library, Scopus, UpToDate. And we extract search results in RIS or CSV format. We remove duplicates by using EndNote, Zotero, or Rayyan AI for screening. We screen and select studies by : a) Title/Abstract Screening: we exclude irrelevant or redundant studies. We include only studies on: a) Uterine septum/arcuate uterus. b) Infertility, implantation failure, or reproductive outcomes c) Randomized controlled trials, observational studies, systematic reviews. Full-text review with download and review all eligible full texts applying Inclusion/Exclusion Criteria. Inclusion: Studies with clear reproductive outcomes (implantation failure, live birth rates). Exclusion: Case reports, editorials, duplicate data, non-English articles (if necessary). We extract data systematically by using a standardized data extraction form (Excel or software like Covidence) including: study details (author, year, country), population characteristics, uterine anomaly classification (ASRM, ESHRE), reproductive outcomes (implantation failure, live birth rates), intervention details (surgical correction vs. no treatment).

**Comparator** Comparison with women without septate or arcuate uterus searching spontaneous pregnancy or by IVF.

**Study designs to be included** Randomized controlled trials (RCTs), prospective non-randomized studies, observational studies, retrospective studies, and systematic reviews with meta-analyses, including Cochrane reviews.

**Eligibility criteria** Search Strategy and Eligibility Criteria A comprehensive literature search was conducted in PubMed, Embase, CINAHL

Complete, MEDLINE, PsycInfo, Global Health, Cochrane Library, Scopus, and UpToDate from 1980 to March 2025. The search terms included "uterine septum," "septate uterus," "arcuate uterus," "infertility," "implantation failure," and "sterility."

**Information sources** PubMed, Embase, CINAHL Complete, MEDLINE, PsycInfo, Global Health, Cochrane Library, Scopus, and UpToDate from 1980 to March 2025. The search terms included "uterine septum," "septate uterus," "arcuate uterus," "infertility," "implantation failure," and "sterility."

**Main outcome(s)** Implantation rates and Live Birth rates.

**Quality assessment / Risk of bias analysis** We assess quality & bias by calculating Risk of Bias (ROBINS-I for observational, Cochrane RoB 2 for RCTs) and generating a color-coded risk-of-bias summary chart. And by evaluation GRADE Assessment as for study quality (high, moderate, low, very low).

**Strategy of data synthesis** Meta-analysis for both implantation rates and live birth rates.

**Subgroup analysis** Spontaneous and IVF pregnancies, arcuate and septate uterine.

**Sensitivity analysis** Meta-analysis and Grade evaluation.

**Language restriction** English.

**Country(ies) involved** Italy.

**Keywords** uterine septum," "septate uterus," "arcuate uterus," "infertility," "implantation failure," and "sterility."

#### Contributions of each author

Author 1 - Francesco Maria Bulletti - conceptualized and supervised the study from data analysis to preparation of the manuscript.

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