Review Article

T-shaped Uterus in the 21st Century (Post DES era) – We Need to Know More!

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Abstract

T-Shaped uterus is a rare uterine malformation, and has classically been associated with "in-utero" exposure of DES (diethylstilbestrol). Surprisingly, the prevalence of T shaped uterus is significant even today. Hysteroscopic metroplasty is a simple procedure which can potentially improve outcomes in sub-fertile women, but the data is not robust. There is a need for centralised database for registration of women with T shaped uterine anomalies, which will help in defining clear diagnostic criteria, surgical indication & technique, and follow up of reproductive outcomes after the procedure.

Keywords: *Dysmorphic uterus, metroplasty, T-shaped uterus*

Introduction

A T-shaped uterus is a rare uterine malformation and has been classically associated with "*in utero*" exposure of diethylstilbestrol (DES).[1] DES is a synthetic estrogen that was prescribed in the 1940s, 1950s, and 1960s to prevent miscarriage and premature delivery. In 1971, the Food and Drug Administration issued a warning against its use in pregnant women after researchers at Massachusetts General Hospital in Boston linked it to a rare cancer of the vagina and cervix – clear-cell adenocarcinoma (CCA) in the daughters of women who took the drug while pregnant.[2,3]

The following conditions are increased in these women:

- CCA – Approximately one in 1000 (0.1%) DES daughters will be diagnosed with CCA. The risk is virtually nonexistent among premenopausal women not exposed to DES
- Reproductive tract structural differences – T-shaped uterus, hooded cervix, cervical cockscomb, and pseudopolyp
- Pregnancy complications – Ectopic pregnancy and preterm delivery
- Infertility.

It has been associated with poor reproductive outcomes when left untreated such as recurrent miscarriage and preterm birth. Reproductive outcome following surgical intervention is not well reported.

Received: 17-07-2019 **Revised:** 24-09-2019
Accepted: 01-11-2019 **Published:** 17-12-2019

Access this article online

Quick Response Code:

Website: www.jhrsonline.org

DOI: 10.4103/jhrs.JHRS_101_19

Hysteroscopic metroplasty is a simple, safe, and relatively quick procedure with advantages of shorter operative time, short hospitalization stay, and decreased incidence of complications as opposed to the previous technique of laparotomy.[4,5] It is, therefore, the procedure of choice when managing patients diagnosed with a T-shaped/dysmorphic uterus. Initial reproductive outcomes following metroplasty in T-shaped uterus have been promising. This article aims to review and analyze the current data and literature around the use of hysteroscopic metroplasty and the reproductive outcomes in the management of T-shaped uterus.

Methods

This study was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. A literature search of the PubMed, Embase, and Cochrane databases was performed using the key T-shaped uterus, dysmorphic uterus, and hysteroscopic metroplasty from inception to September 2018. The reference lists of any identified studies were also reviewed for studies that potentially met the inclusion criteria. No language filters were applied to the search.

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How to cite this article: Sood A, Akhtar M. T-shaped uterus in the 21st century (Post DES era) – We need to know more!. J Hum Reprod Sci 2019;12:283-6.

All studies with clear outcome evaluating the reproductive outcomes in dysmorphic/T-shaped uterus following hysteroscopic metroplasty were included in the study.

Eligibility criteria

- Women diagnosed with T-shaped uterus undergoing hysteroscopic metroplasty
- Hysteroscopic metroplasty only as surgical intervention
- History of poor reproductive outcomes in participants
- Outcomes include live birth rate and miscarriage rate
- Outcomes had to relate specifically to T-shaped/dysmorphic uterus rather than umbrella term of uterine anatomical abnormality, for example, septate uterus.

The primary outcome measure was the pregnancy rate following hysteroscopic metroplasty. The secondary outcome measures were miscarriage rates following procedure and any other adverse outcomes reported.

All studies identified were independently reviewed in full by two researchers in accordance with the PRISMA statement to confirm the eligibility for inclusion, and any disagreements were resolved through discussion and involvement of a third reviewer where necessary. Studies reporting reproductive outcomes in multiple uterine anomalies/intrauterine synechiae were excluded from the study. All studies were at high risk of bias as only case series have been published and no case–control studies or randomized trials have been done. Any discrepancies between the reviewers were discussed and resolved by consensus of both the authors.

Results

A total of 128 articles were identified following database search and one article was identified from reference list. After removing duplicates, 73 articles were screened, and after through screening and assessment for eligibility, 15 articles comprising a total of 790 women who underwent hysteroscopic metroplasty were included in the review. Of these, eight were published articles and seven were conference abstracts. It was agreed to include the abstracts which fit the inclusion criteria.

Table 1 summarizes the data from the included studies, mentioning the author and year of publication, the number of patients included and the reproductive outcomes, the total number of pregnancies achieved in the patients prehysteroscopic metroplasty and after the procedure, and the number of miscarriages prehysteroscopic metroplasty and postprocedure. There is a discrepancy in the data of number of pregnancies, where some studies have included clinical pregnancy and other full-term pregnancies; the distinction has been made in the table.

Pregnancy rates

All the included studies reported pregnancy rates following hysteroscopic metroplasty, though the definition of pregnancy rate is not clear in most studies. Only number of pregnancies achieved was mentioned, and it is not clear if the same patient achieved multiple pregnancies subsequently. The interval between surgery and pregnancy is not clearly defined, and it is difficult to comment if the intervention in the form of hysteroscopic surgery was the reason for improved outcome. Case series are at high risk of bias, and these data must be interpreted with caution.

Miscarriage rates

Miscarriage rates were reported in 11 of 15 studies. Meier *et al*. (2014) and Ehiremen *et al*. (2016) had no pregnancy reported presurgery. A decrease in miscarriage rates was reported in the remaining nine studies.

Other adverse outcomes

The complication rates were low. The most commonly reported complications were ectopic pregnancy, preterm birth, retained placenta, and need for the second procedure.

A systematic review showed a potential benefit from surgical intervention in the form of hysteroscopic metroplasty. It is reported to improve pregnancy rates and live birth rates and concurrently decrease miscarriage rates. It was difficult to derive the meaningful measure of improvement due to potential differences and bias in reporting. Meta-analysis of the data could not be done due to reasons detailed below.

Discussion

It is well known that subfertility and obstetric complications are more common in women with dysmorphic uterus than those with normal uterine cavity. There are scarce data on reproductive outcomes after intervention in the T-shaped/dysmorphic uterus. There is no randomized controlled trial done, and the only studies that are available are mostly retrospective analysis or small number prospective studies. Furthermore, many of these are not published and only presented as conference abstracts.

T-shaped uterus, though classically associated with DES exposure, can be seen as a congenital variant rarely. In the 20th century, the diagnosis of T-shaped dysmorphic uterus was made with hysterosalpingography and two-dimensional ultrasound. As the imaging modalities have now improved, with an increasing

Table 1: Reproductive outcomes following surgical intervention in T-shaped uterus (hysteroscopic metroplasty)

Name of author, year of publication	*n*	Preprocedure pregnancy	Postprocedure pregnancy	Miscarriage preprocedure	Miscarriage postprocedure
Nagel *et al*., 1993	8	0 (FT)	4	10	0
Katz *et al*., 1996[6]	8	0 (FT)	4	10	0
Garbin *et al*., 1998	24	33 (CP)	13	27	1
Barranger *et al*., 2002	29	26 (CP)	30	20	9
Giacomucci *et al*., 2011[7]	17	0 (FT)	21	Data not available	Data not available
Fernandez *et al*., 2011[8]	97	78 (CP)	57	61	16
A Di Spiezio *et al*., 2015[9,10]	30	1 (FT)	17	7	5
Ducellier-Azzola *et al*., 2018[11,12]	112	4 (FT)	60	126	22
Soekoer *et al*., 2016[13] (abstract)	78	75 (CP)	37	63	7
Ehiremen *et al*., 2016 (abstract)	12	0 (FT)	9	0	1
Adriaensen *et al*., 2016[14] (abstract)	103	0 (FT)	77	18	16
Dzotsenidze *et al*., 2015[15] (abstract)	28	0 (FT)	8	Data not available	Data not available
Meier *et al*., 2014[4] (abstract)	100	0 (FT)	57	0	9
De Bruyn C *et al*., 2013[16] (abstract)	56	0 (FT)	45	Data not available	Data not available
Mounir M *et al*., 2012[17] (abstract)	88	0 (FT)	58	Data not available	Data not available

FT=Full-term pregnancy, CP=Clinical pregnancy

use of three-dimensional (3D) USS in gynecology and reproductive medicine, the detection rates and diagnosis of T-shaped/dysmorphic uterus have increased.[18] As 3D technology continues to become more accessible and more providers become proficient in using it, ultrasound may replace magnetic resonance imaging as the new gold imaging standard in diagnosing Müllerian anomalies. In the reproductive population of today's date (age 20–45 years), constitutes all women who were born well after the use of DES was completely stopped. The diagnostic criteria, investigation of choice, reproductive outcomes, and treatment options are not well defined for these women.

The American Society for Reproductive Medicine classification was proposed in 1978, which classified the DES-related anomalies as Class VII. The new ESHRE-ESGE classification has been proposed by the CONgenital UTerine Anomalies Working Group in 2016 which classified the T-shaped and infantilism as Class U1.

Uterine wall thickness is an important parameter and a reference point for the definitions of dysmorphic T-shaped, septate, and bicorporeal uteri according to the new classification system. The adoption of an objective criterion for the definition of uterine deformity is one of the advantages of the new classification system, since according to the American Fertility Society classification, the detection of anomalies was based only on the subjective impression of the clinician performing the test.

The data described above could not be meaningfully analyzed because of the following reasons:

1. No randomized controlled trials
2. No multicentric data
3. Heterogeneous study data – patient population, diagnostic modality, and procedure details
4. Only number of pregnancies achieved was mentioned in most of the studies, and it is not clear if the same patient achieved multiple pregnancies subsequently
5. The interval between surgery and pregnancy is not clearly defined, and it is difficult to comment if the intervention in the form of hysteroscopic surgery was the reason for improved outcome
6. High risk of bias
7. Postoperative uterine synechiae could be detrimental for fertility.

Conclusion

There is a need for centralized database for registration of women with T-shaped uterine anomalies so that we can get meaningful outcome data. This can be either a national or European registry database. This will help in defining clear diagnostic criteria, surgical indication and technique, and follow-up of reproductive outcomes after the procedure.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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