

# Reproductive Outcome of Transcervical Uterine Incision in Unicornuate Uterus

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## Abstract

**Background:** The pregnancy outcome of the unicornuate uterus is associated with an increased risk of miscarriage, cervical incompetence, and a number of obstetric complications. However, at present, there is no accepted treatment method for women with unicornuate uterus, other than expectant measures. The aim of this study was to evaluate the reproductive outcome of transcervical uterine incision (TCUI) in patients with unicornuate uterus.

**Methods:** Thirty-three patients with unicornuate uterus presented to our tertiary center for infertility or miscarriage. All 33 patients underwent TCUI and were followed up for 10–52 months. The pregnancy outcomes (first-trimester miscarriage, second-trimester miscarriage, preterm, term, intrauterine death, ongoing pregnancy, and live birth) before and after TCUI were compared by *t*-test.

**Results:** Among 31 patients who attempted to conceive after TCUI, twenty conceived including one termination of pregnancy, one second-trimester miscarriage, one ectopic pregnancy, five preterm deliveries, 11 term delivery, and one ongoing pregnancy. There were 16 live births in total. There was significant reduction in the first-trimester miscarriage rate ( $t = 4.890$ ;  $P < 0.001$ ), increase in term delivery ( $t = -3.288$ ;  $P = 0.002$ ), and live birth rates ( $t = -4.073$ ;  $P < 0.001$ ) after TCUI.

**Conclusion:** TCUI appeared to improve the pregnancy outcome in women with unicornuate uterus presenting with infertility or miscarriage.

**Key words:** Hysteroscopy; Pregnancy Outcome; Surgery; Transcervical Incision of Uterus; Unicornuate Uterus; Uterine Anomalies

## INTRODUCTION

Unicornuate uterus accounts for 4.4% of all uterine anomalies.<sup>[1]</sup> It is thought to arise from the failure in the development of one of the paramesonephric ducts, either partially (results in a rudimentary horn) or completely (isolated hemiuterus). Coexisting ipsilateral ovarian agenesis has also been reported, suggesting that this anomaly may arise as a consequence of agenesis involving all structures derived from one urogenital ridge.<sup>[2]</sup> Unicornuate uterus is frequently associated with urinary tract anomaly including renal agenesis.<sup>[3]</sup>

In women with unicornuate uterus and a separate rudimentary horn, removal of the rudimentary horn has been advocated in women troubled with severe dysmenorrhea and to avoid rudimentary horn pregnancy. Regardless of whether or not the rudimentary horn is present or has been removed, pregnancy occurring in the unicornuate uterus is associated with an increased risk of first-trimester miscarriage,

second-trimester loss, cervical incompetence, and a number of obstetric complications such as intrauterine growth restriction (IUGR), preterm delivery, malpresentation, and intrauterine death [Table 1]. Specifically, the overall literature data suggest a spontaneous miscarriage rate of 19.5%, preterm delivery rate of 19.1%, and term delivery rate of 21.0%. The exact mechanism responsible for the poor reproductive outcomes in unicornuate uterus is unknown. At present, there is no accepted treatment method for women with unicornuate uterus, other than expectant measures. In this report, we described a consecutive series of 33 cases

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**Table 1: Literature review of reproductive outcome in unicornuate uterus without metroplasty, n**

Author	Year	Subjects	Conceived	Pregnancies	Miscarriage (first/second trimester)	Preterm delivery	Term delivery	Live birth
Baker <i>et al.</i> <sup>[4]</sup>	1953	4	4	5	0/0	0	5	4
Wajntraub <i>et al.</i> <sup>[5]</sup>	1975	1	1	2	0/2	0	0	0
Beernink <i>et al.</i> <sup>[6]</sup>	1976	5	4	8	1/0	3	5	7
Heinonen <i>et al.</i> <sup>[7]</sup>	1982	13	10	15	7/0	3	5	6
Andrews and Jones <sup>[8]</sup>	1982	5	5	13	4/3	1	4	5
Fedele <i>et al.</i> <sup>[9]</sup>	1987	19	13	29	15/2	3	8	11
Golan <i>et al.</i> <sup>[10]</sup>	1990	7	NA	12	0/1	3	8	NA
Stein and March <sup>[11]</sup>	1990	12	NA	16	0/0	5	11	16
Ludmir <i>et al.</i> <sup>[12]</sup>	1990	5	5	5	1/0	1	3	4
Moutos <i>et al.</i> <sup>[13]</sup>	1992	23	20	36	11/2	3	19	21
Donderwinkel <i>et al.</i> <sup>[14]</sup>	1992	45	23	45	10/7	8	20	28
Acién <sup>[15]</sup>	1993	23	21	55	10/2	9	33	40
Heinonen <sup>[16]</sup>	1997	42	36	93	13/2	10	48	57
Raga <i>et al.</i> <sup>[17]</sup>	1997	8	NA	16	6/1	4	5	7
Dicker <i>et al.</i> <sup>[18]</sup>	1998	1	1	2	0/0	1	0	1
Daskalakis <i>et al.</i> <sup>[19]</sup>	2002	1	1	3	1/1	0	0	0
Airoldi <i>et al.</i> <sup>[20]</sup>	2005	12	NA	12	NA	2	NA	NA
Akar <i>et al.</i> <sup>[21]</sup>	2005	55	38	65	9/10	28	15	19
Haydardedeoglu <i>et al.</i> <sup>[22]</sup>	2006	1	1	3	0/1	0	3	3
McAvey and Chasen <sup>[23]</sup>	2009	19	NA*	39	14/0	17 <sup>†</sup>	NA	NA
Anderson and Chasen <sup>[24]</sup>	2013	27	NA	37	0/1 <sup>‡</sup>	10 <sup>§</sup>	NA	NA
Watson <i>et al.</i> <sup>[25]</sup>	2013	120	NA	341	NA	62	NA	227
This study	2017	33	28	69	43/0	3	1	4
Total		486	211	921	180 (19.5) <sup>  </sup>	176 (19.1) <sup>  </sup>	193 (21.0) <sup>  </sup>	460 (49.8) <sup>  </sup>

\*Data retrieved from obstetrics database; †Included both preterm delivery and second-trimester miscarriage; ‡Only pregnancies >12 weeks were included in this study; §Five cases were spontaneous preterm deliveries, five were iatrogenic preterm deliveries; ||The data were presented by n (%). NA: Not available.

of unicornuate uterus treated by a novel surgical technique, transcervical uterine incision (TCUI), designed to widen the narrow uterine cavity, to test the hypothesis that the adverse pregnancy outcome associated with unicornuate uterus is related to the reduced capacity of the uterine cavity in this group of women.

## METHODS

A consecutive series of 33 infertile patients with unicornuate uterus who had been excluded from other infertility factors admitted to the hospital from January 2010 to December 2014 were included in this study, which is approval of the Independent Ethics Committee of Fu Xing Hospital, Capital Medical University and also obtained informed consent from all of the research participants. The diagnosis was confirmed in all cases with three-dimensional ultrasonography, as well as combined laparoscopy and hysteroscopy. TCUI was carried out under general anesthesia in all 33 subjects. Clinical data were reviewed from each of the patients' hospital record, and the follow-up of their reproductive outcome after TCUI was collected through a phone call at regular intervals. The duration of follow-up ranged from 10 to 52 months postoperation.

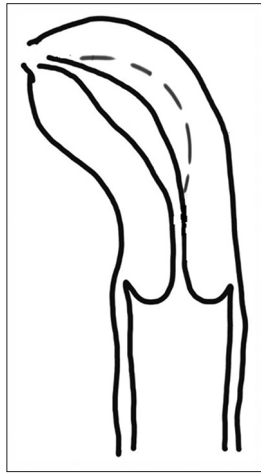
## Surgical details

The night before TCUI, cervical dilating stick was inserted into the uterine canal to let the cervical canal soft and dilated. TCUI was designed to resect the opposite uterine wall of

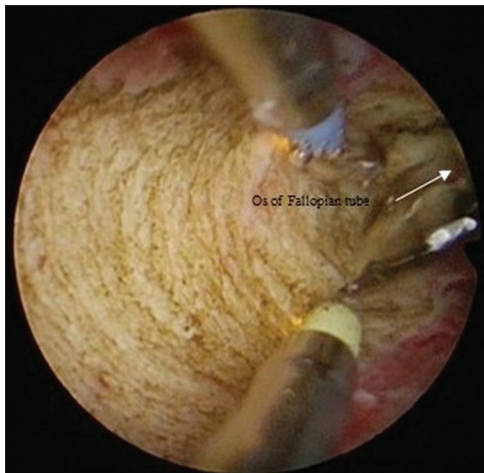
unicornuate horn side [Figure 1]. The patient was put under general anesthesia and placed in lithotomy position. Under the laparoscopic guidance, a Foley catheter was inserted for continuous drainage and the laparoscope (Olympus Medical Systems Corp., Tokyo, Japan) was introduced through a 10-mm umbilical port and pneumoperitoneum was obtained with an insufflation pressure of 15 mmHg (1 mmHg = 0.133 kPa). Under ultrasound guidance, the bladder was full in 200–300 ml sterile normal saline and abdominal ultrasonography (Siemens Healthineers, Berlin, Germany) was used during surgery. Both guidance methods were used to avoid the risk of uterine perforation.

The cervix was dilated to Hegar 10–11, and hysteroscopic bipolar electroresectoscope (Olympus Medical Systems Corp., Tokyo, Japan) was inserted into the uterine cavity with 0.9% normal saline distention media under 100 mmHg distention pressure.

TCUI commenced with a shallow transverse incision over the narrowed fundal part of the unicornuate horn was made using a wire loop or needle electrode. This created a new uterine fundus with a width of  $\geq 2$  cm. Then, a 4-cm long vertical incision was made over the lateral wall [Figure 2], approximately 1 cm deep over the fundal region but taper to stop at the level of the isthmus. After the operation, an inverted triangular-shaped uterine cavity was created [Figure 3]. A Foley catheter was inserted into the uterine cavity after the operation, stayed *in situ* for 5–7 days, and then removed.



**Figure 1:** The incisions of transcervical uterine incision procedure. The dotted line is the incision.



**Figure 2:** A 4-cm long vertical incision was being made over the right lateral uterine wall of a left unicornuate uterus. The arrow means orifice of the fallopian tube.



**Figure 3:** A panoramic view of the cavity of the left unicornuate uterus at the end of the transcervical uterine incision.

Artificial menstrual cycle treatment with estrogen and progesterone was used for two cycles. The second look was performed one month later after surgery.

## Outcome measures

The patients were regularly followed at the outpatient clinic or by telephone contact. The outcome of any pregnancy was documented.

## Statistical analysis

Statistical analysis was performed using statistical package for the social sciences (IBM SPSS Statistics for Windows, Version 22.0, New York, USA). Data were presented as mean  $\pm$  standard deviation (SD). The pregnancy outcomes (first-trimester miscarriage, second-trimester miscarriage, preterm, term, intrauterine death, ongoing pregnancy, and live birth) before and after TCUI were compared by *t*-test.  $P < 0.05$  was considered statistically significant.

## RESULTS

Among 33 patients with unicornuate uterus, 18 patients presented with infertility, whereas the remaining 15 patients presented with miscarriage(s). Their age ranged from 21 to 40 ( $30.3 \pm 4.8$ ) years. There were a total of 69 pregnancies before TCUI, which included 16 termination of pregnancies, 43 first-trimester miscarriages, three ectopic pregnancies, no second-trimester miscarriage, three preterm deliveries, three intrauterine deaths, and one term delivery. In total, there were four live births [Table 2]. However, all the four live births ended in neonatal death.

Among 33 women, 17 had left unicornuate uterus and the remaining 16 had right unicornuate uterus. In addition, 31 cases had rudimentary horn, but two cases did not. For the associated abnormalities, there were three cases of absent or rudimentary tube, one case of absent kidney, and one case of ectopic kidney on the same side of the rudimentary horn. Both ovaries were present in all cases, except one case in whom the left ovary was removed earlier because of dermoid cyst.

Among the 33 cases of TCUI, 27 cases were performed under the laparoscopic guidance and six cases under ultrasound guided. Among 27 patients who underwent laparoscopy, 24 of them had patent tube on the unicornuate side, two had blocked tubes on the unicornuate side (one become patent after fimbrioplasty), and one had absent tube as a result of previous salpingectomy for tubal pregnancy on the unicornuate side. Ten subjects also underwent concomitant surgery, including hysteroscopic division of intrauterine adhesions ( $n = 6$ ), removal of endometrial polyp ( $n = 4$ ), and ablation of endometriotic deposits ( $n = 2$ ) (multiple entry). The blood loss was  $12.0 \pm 8.5$  (range 5.0–50.0) ml, and the operative time was  $42 \pm 21$  (range 15–85) min. There were no intraoperative complications encountered.

Among 33 patients, two wished to defer starting a new family after the operation for personal reasons. For the remaining 31 patients who tried to conceive, twenty women conceived (13 spontaneously, seven with the help of *in vitro* fertilization [IVF]), with the following pregnancy outcomes: One termination of pregnancy at

**Table 2: Comparison of the pregnancy outcome before and after TCUI among the 33 women underwent TCUI**

Pregnancy outcome	Infertility, <i>n</i>		<i>t</i>	<i>P</i>	Miscarriage, <i>n</i>		<i>t</i>	<i>P</i>	Overall, <i>n</i>		<i>t</i>	<i>P</i>
	Pre-TCUI	Post-TCUI			Pre-TCUI	Post-TCUI			Pre-TCUI	Post-TCUI		
Pregnancy	14	10	NA	NA	36	8	NA	NA	50*	18 <sup>†</sup>	NA	NA
First-trimester miscarriage	13	0	3.198	0.005	30	0	4.273	0.001	43	0	4.890	<0.001
Second-trimester miscarriage	0	0	NA	NA	0	1	-1.00	0.334	0	1	-1.00	0.325
Preterm	0	2	-1.458	0.163	3	3	0	1.000	3	5	-0.812	0.423
Term	0	8	-3.688	0.002	1	3	-1.00	0.334	1	11	-3.288	0.002
Intrauterine death	1	0	1.00	0.331	2	0	1.468	0.164	3	0	1.789	0.083
Live birth	0	10	-4.610	<0.001	4	6	-1.382	0.189	4	16 <sup>‡</sup>	-4.073	<0.001
Ongoing pregnancy	NA	0	NA	NA	NA	1	NA	NA	NA	1	NA	NA

\*There were 16 termination of pregnancies and three ectopic pregnancies before TCUI not included in the table; <sup>†</sup>There were one termination of pregnancy and one ectopic pregnancy after TCUI not included in the table; <sup>‡</sup>Two sets of twins, total of 18 babies. NA: Not available; TCUI: Transcervical uterine incision.

9 weeks gestation for severe proteinuria due to nephritis, one second-trimester miscarriages due to cervical incompetence, one ectopic pregnancy, five preterm deliveries, and 11 term deliveries [Table 2]. There were altogether 16 live births. The live birth rate after TCUI was 16/18, which was significantly higher than the rate 4/50 before TCUI ( $t = -4.073$ ,  $P < 0.01$ ), when the whole group of subjects ( $n = 33$ ) is considered. In the same table, the pregnancy outcome data before and after surgery are separately analyzed for women presenting primarily with infertility or miscarriage. Among twenty patients who conceived after TCUI, the pregnancy outcomes before and after TCUI are compared in Table 3. The live birth rate among pregnancies after TCUI (16/18) was also significantly higher than the rate of 3/29 before the operation ( $t = -6.658$ ,  $P < 0.001$ ). The average gestation of delivery after the operation was  $38.0 \pm 1.5$  weeks of gestation (ranged from 35.0 to 40.0 weeks). More than 80% were delivered by lower segment cesarean section (13 out of 15), only two of them delivered vaginally.

For the neonatal outcome, all four live births before TCUI had neonatal death, whereas all 16 live births after TCUI survived beyond 28 days. The mean birth weight of babies born after TCUI was  $2725.0 \pm 832.7$  g (ranged from 800.0 to 4000.0 g). All babies born at term had birth weight  $\geq 2500.0$  g.

There were 11 patients who failed to conceive after TCUI: Seven with coexisting infertility factors (two with male factor, one with anovulation, one with adenomyosis, and three with significant intrauterine adhesions) present before TCUI whereas the underlying cause of infertility was unexplained in the remaining four cases. Women in this group were not ready to proceed with IVF treatment.

## DISCUSSION

Patients with unicornuate uterus may present with infertility, cervical incompetence, and preterm deliveries. The prevalence of primary infertility in these patients had been reported to be 15%.<sup>[26]</sup> In our series, the reproductive outcomes before surgery were much poorer than the literature

review, with a live birth rate of only 5% compared with the literature average of 49.8%. This could be due to selection bias as only women with a poor reproductive history (no surviving baby) were referred to our center. We report here our experience of a novel surgical approach, TCUI, as a form of treatment for women with unicornuate uterus presenting with infertility or miscarriages. While we have shown that the miscarriage rate was reduced and live birth rate increased in our cohort, a reference to the literature data summarized in Table 1 showed that the miscarriage rate and live birth rate after TCUI also appeared to be lower and higher than the mean rates derived from the literature review, respectively.

Congenital uterine anomalies have been associated with infertility, miscarriage, IUGR, and preterm birth. It was suggested to be caused by restricted expansion of an abnormal endometrial cavity and abnormal placental implantation.<sup>[27]</sup> Markham and Waterhouse<sup>[28]</sup> believed that patients with unicornuate uteri were not candidates for surgical reconstruction. On the contrary, our previous article<sup>[29]</sup> reported three live births in unicornuate uterus after TCUI, suggesting that TCUI could improve the pregnancy outcomes of unicornuate uterus by enlarging the uterine cavity. The present study showed a statistically significant improvement in the first-trimester miscarriage, term delivery, and live birth rate after TCUI. Subgroup analysis also showed significant improvement in first-trimester miscarriage, term delivery, and live birth rate in those patients with infertility. However, in the miscarriage group, there was significant improvement in the first-trimester miscarriage rate only, but not the term delivery and live birth rates. This could be explained by the relatively small sample size.

Concerning preterm delivery in our study, although there were five preterm deliveries, two of them were iatrogenic preterm deliveries due to obstetrics cholestasis and pregnancy-induced hypertension at 35 weeks and 36 weeks, respectively. These two cases were both IVF twin pregnancies. There was one case of preterm delivery at 25<sup>+5</sup> weeks due to cervical incompetence, and the



**Table 3: A comparison of the pregnancy outcome before and after TCUI in twenty women who conceived after TCUI, n**

Pregnancy outcome	Before TCUI	After TCUI	t	P
Pregnancy	29*	18†	NA	NA
Miscarriage				
First-trimester miscarriage	25	0	4.626	<0.001
Second-trimester miscarriage	0	1	-1.000	0.330
Preterm	3	5	-0.809	0.428
Term	0	11	-4.819	<0.001
Intrauterine death	1	0	1.000	0.330
Ongoing pregnancy	NA	1‡	NA	NA
Live birth	3	16	-6.658	<0.001

\*There were 11 termination of pregnancies and three ectopic pregnancies before TCUI not included in the table; †There were one termination of pregnancy and one ectopic pregnancy after TCUI not included in the table; ‡Currently, 17 weeks gestation. NA: Not available; TCUI: Transcervical uterine incision.

baby passed away on the 28<sup>th</sup> day of life due to extreme prematurity. The remaining two cases were delivered at 36 weeks due to premature rupture of membranes. Six out of seven neonates survived.

According to Roddick *et al.*,<sup>[30]</sup> cervical incompetence is caused by an abnormal ratio of muscle fibers to connective tissue in the uterine cervix. This is commonly seen in women with congenital uterine anomalies who have a greater proportion of muscle fibers with loss of connective tissue.<sup>[31]</sup> Moreover, asymmetric downward force exerted by an abnormal uterus, which would be even greater when pregnancy occurs, also plays a role in causing cervical incompetence. TCUI perhaps can correct the above two factors by removing the excessive muscle bulk and restore the symmetry of uterus. In our study, among those who conceived after TCUI, 3 (15%) of them had cervical incompetence, which is somewhat lower than the reported 30% incidence of cervical incompetence in the congenital uterine anomaly.<sup>[10]</sup> One patient had successful term delivery after transvaginal cerclage at second trimester, one had miscarriage at 20 weeks, the other case had delivered a live birth at 25<sup>+5</sup> weeks, but the baby died on the 28<sup>th</sup> day of life.

It had been reported that among all uterine anomalies, unicornuate uterus had the highest rate of cervical shortening and the highest rate of spontaneous preterm birth when the cervix is shortened.<sup>[20]</sup> There is currently no convincing evidence that routine cervical cerclage should be performed in women with Müllerian anomaly.<sup>[32]</sup> Instead, cervical length should be monitored with serial transvaginal ultrasound examinations, and elective cervical cerclage should be considered for those with cervical length <25 mm.

Even after TCUI metroplasty, patients with unicornuate uterus were still at high risk of preterm delivery. In our study, the preterm delivery rate after TCUI remained high at 27%. Thus, it is important that patients who conceived after TCUI be managed in high-risk obstetrics units with regular monitoring of cervical length.

In our series, there is one case suffered from primary infertility and right unicornuate uterus and left rudimentary horn in which ultrasonography shown endometrium inside the small cavity. The left kidney is absent. Laparoscopic resection of left rudimentary horn and TCUI for right unicornuate uterus was performed meanwhile under general anesthesia. The patient got pregnancy by IVF. A 3400 g healthy female infant was delivered by cesarean section at 38 gestational weeks. Pregnancies in women after laparoscopic excision of rudimentary horns should be considered as high-risk ones and should be managed accordingly to ensure a satisfactory obstetric outcome.<sup>[33]</sup> Akdemir reported coring-type rudimentary horn removal method which can remain more myometrial tissue, thus more adequate edges for suturing are preserved, which is safer to go through the pregnant course to term.<sup>[34]</sup>

TCUI appears to improve the pregnancy outcome in women with unicornuate uterus, by reducing the first-trimester miscarriage rate and increasing the term delivery and live birth rates. The preterm delivery rate after TCUI remained high. Prospectively planned studies are required to confirm the benefit of TCUI, in particular, to establish whether or not the procedure should only be considered in women with an adverse reproductive history such as the cohort reported in this series.

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### Conflicts of interest

There are no conflicts of interest.

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