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SYSTEMATIC REVIEW

Maternal and perinatal outcomes of live births after uterus transplantation: A systematic review

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Abstract

Introduction: Uterus transplantation (UTx) is a treatment for absolute uterine factor infertility. The results of pregnancies of this complex infertility treatment should be established. The aim of the study was to systematically review maternal and neonatal outcomes in the pregnancies of women who have undergone UTx.

Material and Methods: The population of this review were women that have undergone UTx and delivered child(ren). Cesarean delivery after UTx were planned to be compared with studies reporting maternal mortality/morbidity and perinatal mortality/morbidity after delivery by elective cesarean section without UTx. Systematic literature searches were performed utilizing Medline, Embase, the Cochrane Library, Cinahl, PsycInfo, Web of Science, and clinicaltrials.gov for studies written in English language and published between January 1, 2010, and November 08, 2023. No study design limitation was applied. If no comparative studies were identified, we planned to report the outcomes from the case reports and case series. Included studies were assessed for risk of bias using a checklist for case series. The study protocol was registered with the International Platform of Registered Systematic Review and Meta-analysis Protocols (registration number: INPLASY202310052).

Results: Twenty-four articles were identified, containing data on 40 unique live births. Multiple publications including same cases were identified and clearly indicated. No comparative studies were identified. The certainty of evidence was very low, as all studies were either case reports ($n=15$) or case series ($n=9$). All deliveries were by cesarean section and 47.5% of them resulted in emergency cesarean sections. Out of the 21 elective cesarean sections, 52.4% were performed before 37 weeks' gestation. Historical comparison to population data on pregnancies delivered by cesarean section found a markedly increased risk for both the mother and child following cesarean section for UTx. Risks for placenta previa and preterm birth were notably high after UTx; however, some of the later may reflect the results of provider-initiated births.

Abbreviations: CPAP, continuous positive airway pressure; ICP, intrahepatic cholestasis of pregnancy; IS, immunosuppression; IVF, in vitro fertilization; MRKHs, Mayer-Rokitansky-Küster-Hauser syndrome; NICU, neonatal intensive care unit; PAS, placenta accreta spectrum; PE, preeclampsia; PROM, premature rupture of membranes; PPROM, preterm premature rupture of membranes; PTL, preterm labor; UTx, uterus transplantation.

Conclusions: The maternal and perinatal outcomes of 40 live births post-UTx indicate that these pregnancies may be at high risk of maternal and perinatal complications. Aiming to delay elective cesarean section beyond 37 weeks' gestation could potentially reduce some of these risks. Registration of maternal and perinatal outcomes after UTx through quality registries are essential and obstetrical care guidelines for these women should be established.

KEYWORDS
absolute uterine factor infertility, child, delivery, infertility, maternal, morbidity, mortality, neonate, perinatal, pregnancy, transplantation, uterus

1 | INTRODUCTION

For many decades, absolute uterine factor infertility (AUFI) was considered the ultimate challenge in the field of infertility treatment. The AUFI condition arises from the absence of a uterus or the inability of a present uterus to sustain a pregnancy for a duration that permits neonatal viability. In September 2014, the first live birth after uterus transplantation (UTx) took place from a woman with AUFI due to congenital uterine absence as part of the Mayer-Rokitansky-Küster-Hauser syndrome (MRKHs).[1] She had undergone UTx within the first clinical UTx trial with nine live donor UTx procedures in Sweden during 2012–2013.[2] The first live birth following a UTx procedure with a deceased donor occurred in Brazil in December 2017.[3] Data from a recent comprehensive review on UTx[4] provides information on the surgical outcome of 71 UTx procedures published until the fall of 2022, albeit excluding most pertinent data on maternal and perinatal outcomes.

A pregnancy after UTx is the final stage of a serial and protracted procedure involving very complex procurement surgery of the uterus, uterine ischemia and reperfusion injury, intricate vascular anastomosis surgery in the recipient, pregnancy by in vitro fertilization (IVF) with embryo transfer, and fetal exposure to maternal immunosuppression (IS). Thus, there are several factors that may negatively affect pregnancy outcomes in women with uterine allografts.

It is crucial to monitor the outcomes of these unique pregnancies to understand the potential consequences for both mothers and children in forming the basis for development of guidelines for pregnancy and postnatal follow-up after UTx. It is recognized that IS may pose pregnancy risks for both the fetus and the mother. To date there are examples of IS-exposed pregnancies of women that have undergone solid organ transplantation and the data from large registries show that women under IS carry increased risks for obstetrical complications, such as fetal growth restriction, prematurity, and low birthweight, as reviewed by Ponticelli et al. 2018.[5] However, one publication carrying data of the entire cohort of transplanted women in Sweden who had given birth showed that the high rates of obstetrical complications were equally common in pregnancies of these women before transplantation, which could indicate that there are patient-specific factors other than IS that might influence the obstetrical outcome.[6] Additionally, it should be noted that women with uterine grafts are often slightly older at first childbirth compared to the general population and that some UTx women carry uteri of peri- or post-menopausal age,[2] raising concerns about the influence of maternal age-associated higher risks of preterm labor (PTL), gestational diabetes, preeclampsia (PE), and adverse fetal outcomes such as fetal growth restriction.[7] The aim of the study was to systematically review maternal and neonatal outcomes in the pregnancies of women who have undergone UTx.

Key message

Pregnancies and live births after uterus transplantation are at high-risk of maternal complications such as hypertensive disorders and premature rupture of membranes, as well as perinatal complications including preterm birth and respiratory distress syndrome.

2 | MATERIAL AND METHODS

This systematic review was performed according to the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)[8] using the INPLASY registration number INPLASY202310052.

2.1 | Data sources and eligibility criteria

Literature searches were conducted on December 22, 2022 and updated November 8, 2023, in the following databases: Medline, Embase, the Cochrane Library, Cinahl, PsycInfo, and Web of Science. These searches were executed by a medical librarian who employed a combination of controlled vocabulary and free-text terms (see Figure S1). Only publications in English language published from January 1, 2010, were included, since it is well-verified that the first live birth after UTx took place in 2014.[1] Prior to 2010, only one UTx procedure had been performed and that was a case with graft failure

after 3 months.[9] In order to identify additional references, the reference lists of relevant articles were carefully reviewed. In the initial screening process, three independent reviewers individually assessed all abstracts and, if necessary, reviewed full-length articles. Any disagreements were resolved through consensus, as outlined in Figure S2.

The remaining potentially eligible articles were shared with all authors for assessment. Exclusions were made based on the articles not meeting the research question, such as conference abstracts or forms other than original articles. The PICO criteria (Figure 1) ensured that no specific study design limitations were imposed during the search, meaning that case reports and case series without comparators were included. Disagreements in the assessment of articles were resolved through consensus among the authors.

On December 22, 2022, and November 8, 2023, updated searches were conducted in Clinicaltrials.gov using the search terms "uterus transplant* OR uterine transplant* AND (cesarean OR caesarean OR parturition OR parturitions OR birth OR births OR livebirth OR livebirths OR childbirth OR childbirths OR delivery OR deliveries)," which identified 30 trials. Of these, seven studies were deemed relevant and are listed in Table S1.

2.2 | Main outcomes and measures

The population of this review were women that have undergone UTx and delivered child(ren). Cesarean delivery after UTx were planned to be compared with studies reporting maternal mortality/morbidity and perinatal mortality/morbidity after delivery by elective cesarean section without UTx. Outcomes of interest were perinatal mortality, short-term perinatal outcome (admission to neonatal unit), hypoxic ischemic encephalopathy or need for therapeutic hypothermia/seizures, asphyxia defined as Apgar score <5 at 5 min, meconium aspiration syndrome (MAS), need for respiratory support by continuous positive airway pressure (CPAP)/respirator, respiratory distress syndrome (RDS), pulmonary adaption disorder, neonatal infection, fetal malformation, disability, preterm birth, fetal growth restriction as defined as fetal weight <10th percentile or <2 SD according to Marsal et al.[10] and disability/neurodevelopmental delay diagnosed at 2 years follow up. Maternal outcomes included maternal mortality and short-term maternal outcome (cardiorespiratory arrest, hysterectomy for any complications related to birth, intensive care unit admission, pulmonary embolism, stroke, hemorrhage >1000 mL, chorioamnionitis or other maternal infections, pulmonary embolism, gestational hypertension (GH), gestational diabetes, placenta previa, placenta accreta spectrum (PAS), hydronephrosis requiring stenting, intrahepatic cholestasis of pregnancy (ICP), premature rupture of membranes (PROM), length of hospital stay, and postnatal depression).

2.3 | Data collection and analysis

The individual data for all outcomes were extracted independently by three authors from published reports only. None of the authors of

PICO (Patient, Intervention, Comparison and Outcome)

Research question: Is delivery by elective cesarean section as safe for the mother and the neonate after uterus transplantation as after delivery by elective cesarean section for reasons such as breech and psychological indication regarding stillbirth/neonatal mortality, neonatal morbidity, maternal mortality, and morbidity?

P Women that have undergone uterus transplantation and delivered child(ren)

I Delivery after uterus transplantation

C Delivery by elective cesarean section (such as breech, psychological indication etc.)

O 1) Perinatal outcomes

Death, hypoxic ischemic encephalopathy (HIE) or need for therapeutic hypothermia/seizures, admission to neonatal unit, meconium aspiration syndrome (MAS), need for respiratory support/ continuous positive airway pressure (CPAP)/respirator, neonatal infection, respiratory distress syndrome (RDS), fetal malformation, disability including neurodevelopmental delay including two years follow up, preterm birth <37 gestational weeks, fetal growth restriction (FGR) <10th percentile and <2 SD.

2) Maternal outcomes

Maternal mortality, cardiorespiratory arrest, hysterectomy for any complications related to birth, intensive care admission, pulmonary embolism, stroke, hemorrhage >1000ml, chorioamnionitis and other maternal infections, preeclampsia (PE), gestational hypertension (GH), hypertension, diabetes, placenta praevia, placenta accreta spectrum (PAS), hydronephrosis demanding stenting, intrahepatic cholestasis of pregnancy (ICP), premature rupture of membranes (PROM), length of hospital stay (LOS), postnatal depression.

No limitations as regards to study design. English only. Publication date from January 1st, 2010. Databases: Medline, Embase, the Cochrane Library, Cinahl, PsycInfo and Web of Science, www.clinicaltrials.gov

FIGURE 1 The PICO model to define the population, intervention, comparison, and outcome was used.

TABLE 1 Excluded articles ($n = 23$) and reasons for exclusion.

Author, year, country	Title, details of publication/presentation	Exclusion reason
Brännström M, et al., 2015, Sweden	Uterus transplantation with live births-an update. Abstract no 84, presented at 54th Annual Meeting of the European Society for Pediatric Endocrinology, Barcelona, Spain. Horm Res Paediatr 2015; Suppl. 1:1–662	Congress abstract
Brännström M, et al., 2015, Sweden	Live birth after uterus transplantation. Obstetrical & Gynecological Survey 2015;70:394–395	Editorial commentary
Johannesson L, et al., 2018, USA	First birth after uterus transplant in the US. Abstract no 283, presented at 2018 American Transplant Congress, Seattle, USA.	Congress abstract
Johannesson L, et al., 2020, USA	Live births after uterus transplantation: report of the first six deliveries at a single center-Duets (Dallas Uterus Transplant Study). Abstract P-383, presented at 76th Congress of the American Society for Reproductive Medicine, virtual congress, USA. Fertil Steril 2020;114: e261-e262	Congress abstract
Putman JM, et al., 2020, USA	In vitro fertilization and pregnancy outcomes after uterus transplantation: Duets (Dallas Uterus Transplant Study). Abstract P-896 presented at 76th Congress of the American Society for Reproductive Medicine, virtual congress, USA. Fertil Steril 2020;114:e471	Congress abstract
Daolio J, et al., 2020, Italy	Uterine transplantation and IVF for congenital or acquired uterine factor infertility: a systematic review of safety and efficacy outcomes in the 52 recipients. PLOS ONE 2020;15: e0232323	Review. Wrong outcome
Quintini C, et al., 2020, USA	Outcomes in cadaveric uterus transplantation. Abstract no 505, presented at 2020 American Transplant Congress, Philadelphia, USA.	Congress abstract
Testa G, et al., 2020, USA	The evolution of transplantation from saving lives to fertility treatment: DUETS (Dallas UtErus Transplant Study). Ann Surg 2020; 272:411–417	Original data reported in included articles
Putman JM, et al., 2021, USA	Clinical pregnancy rates and experience with in vitro fertilization after uterus transplantation: Dallas Uterus Transplant Study. Am J Obstet Gynecol 2021; 225:155.e1-155.e11	Wrong outcome
Eagle E, et al., 2021, USA	Pregnancy outcomes following uterus transplant. Abstract no 917, presented at Society for Maternal-Fetal Medicine 41st Annual Meeting, Las Vegas, USA. Am J Obstet Gynecol 2021;224: s570	Congress abstract
Del Prete L, et al., 2021, USA	Cleveland clinic experience with cadaveric uterus transplant. Abstract no 374, presented at 2021 American Transplant Congress, virtual congress, USA.	Congress abstract
Sheata IM, et al.,2021, Egypt	Anesthetic considerations for cesarean delivery after uterine transplant. Cureus 2021;13:13920	Wrong outcome
Jana J, 2021, India	Anesthesia for cesarean section after uterine transplant-Indian Experience. Anesth Analg 2021	Wrong outcome
Johannesson L, et al., 2022, USA	Living donor robotic hysterectomy provides excellent outcomes in uterus transplant recipients. Abstract no 462, presented at 2022 American Transplant Congress, Boston, USA	Congress abstract
Perni UC, et al., 2022, USA	Antepartum care of the uterus transplant patient: the experience of 3 successful US centers. Clin Obstet Gynecol 2022;65:84–91	Commentary
Richards EG, et al., 2022, USA	Surgical and reproductive outcomes in a large deceased donor uterus program: Cleveland Clinic's six-year report. Abstract no E33, presented at 78th Congress of the American Society for Reproductive Medicine, Anaheim, USA. Fertil Steril 2022; 118: e33	Congress abstract
Johannesson L, et al., 2022, USA	The first 5 years of uterus transplant in the US: a report from the United States Uterus Transplant Consortium. JAMA Surgery 2022; 157:790–797	Review. Group data
Ozkan O, et al., 2022, Turkey	Comment on "Birth of a healthy baby 9 years after a surgically successful deceased donor uterus transplant": Erratum. Ann Surg 2022;276:e264	Erratum, typo of author name
Slomski A, 2022, USA	Uterus transplant a clinical reality. JAMA 2022;328:817	Commentary
Johannesson L, et al., 2023, USA	Neonatal outcomes after uterus transplantation: Dallas uterus transplant study. Am J Perinatol 2023;40:4250	Congress abstract
Wilson NK, et al., 2023, USA	Immunosuppression in uterus transplantation: experience from the Dallas uterus transplants. Transplantation 2023;107:729–736	Wrong outcome

TABLE 1 (Continued)

Author, year, country	Title, details of publication/presentation	Exclusion reason
Author unknown, 2023, India	World's first birth after uterus transplantation with robot-assisted surgery alone. Indian Practitioner 2023	Unavailable
Johannesson L, et al., 2023, USA	The first 5 years of uterus transplant in the US-a report from the United States uterus transplant consortium. Obstetrical & Gynecological Survey 2023;78:139–141	Editorial commentary

the included articles were contacted. A specific live birth which was reported in more than one study and with different sets of outcomes, were identified as a unique birth when gestational length, gender at time of birth, and Apgar score/weight were identical. To ensure accuracy, this was also verified by center-specific data presented at the yearly (since 2017) scientific meetings of the International Society of Uterus Transplantation (ISUTx).

At least two authors independently appraised the included studies using a checklist for case series used by the Health Technology Assessment-center at Sahlgrenska University Hospital, modified from checklists developed by the Swedish Agency for Health Technology Assessment and Assessment of Social Services.[11] Consensus discussions were then held to review the biases in the case series. The domains of directness, study limitations (risk of bias), and precision were evaluated. Each category was rated as + (no or minor problems), (some problems), or (major problems). In all calculations, the total number of live births ($n=40$) were used in the denominator, with an assumption that if not reported in the article, it implies negation. However, non-reported data could also imply a risk of bias in that specific study. In the detailed outcome tables (Tables 3 and 4), only data presented in the articles are specified. Non-reported data are indicated as NR (not reported). In the event that a specific item is not reported in any article at all, the item is not included in Tables 3 and 4.

3 | RESULTS

We identified 24 articles after the removal of duplicates. No studies with comparative analyses were found. Therefore, as planned a priori, case reports and case series involving the intervention were included. A total of 454 exclusions were made at abstract level and an additional 23 at full-text level, as depicted in Figure S2. The excluded full-text articles and the reasons for exclusion are outlined in Table 1.

The included 24 articles, all of which were case reports or case series, were assessed by three of the authors. The final assessment incorporated data from 40 live births occurring in 36 women.[1,3,12–33] These studies are listed in Table 2, including presented maternal and perinatal outcome variables. Overall, the certainty of evidence was very low, largely owing to the case study and case series designs in all included studies. The assessments regarding directness and study quality (risk of bias) of the case series are presented in Table 2. Several live births were reported with partial information in more than one article. Thus, partial data of three unique births were reported in four different articles, partial data of nine unique births were reported in three different articles, and partial data of six unique births were reported in two different articles.

3.1 | Maternal outcomes

The available data for maternal outcomes are given in detail in Table 3. The rate of hypertensive disorders of pregnancy was 9/40 (22.5%), with 3/40 (7.5%) and 6/40 (15.0%) of pregnancies complicated by GH and PE, respectively. Gestational diabetes and ICP were identified in 3/40 (7.5%) and in 2/40 (5.0%) of pregnancies, respectively. Placental complications involving PAS were observed in 2/40 cases (5.0%) and placenta previa occurred in 4/40 cases (10.0%). One case from the placenta previa group exhibited both placenta previa and PAS. Premature rupture of membranes was present in 4/40 (10%) of cases.

All deliveries were singleton and by cesarean section, with 21/40 (52.5%) being elective and 19/40 (47.5%) were emergency cesarean section. The reasons for emergency cesarean section varied; single factors motivating emergency cesarean section were PTL in eight cases, PE in three cases, PROM in one, preterm PROM (PPROM) in one, acute kidney injury in two cases and ICP in one case. A combination of two factors leading to emergency cesarean section was identified in two cases (one with PE+ fetal growth restriction; one with PPROM+PTL). A combination of three factors leading to emergency cesarean section was identified in one case of PPROM+ICP+PE. Maternal length of hospital stay was reported for 12 live births, showing a median of 4 days (range 2–48 days).

Most studies had not reported data on the outcomes chorioamnionitis or other infections during pregnancy, hemorrhage > 1000 mL, and admission to intensive care unit. There were no reported events of the maternal outcomes of hydronephrosis demanding stenting, pulmonary embolus, stroke, cardiorespiratory arrest, postnatal depression, and death.

3.2 | Perinatal outcomes

The perinatal outcomes of the 40 children are given in Table 4. The total rate of preterm birth before 37 weeks was 28/40 (70.0%), with 11/28 (39.3%) of preterm births following elective cesarean sections. These 11 preterm elective cesarean sections were at 34 ($n=1$), 35 ($n=5$) and 36 ($n=5$) weeks of gestational age. All but one of the 19 emergency cesarean sections were at preterm gestation, with two of these occurring at gestational week of 28 weeks (Table 4).

TABLE 2 Included articles ($n = 24$) with evaluation of bias for case series.

Number, author	Study design/number of live births	Directness	Study limitations	Precision	Included maternal variables	Included perinatal variables
1. Brännström, et al. Livebirth after uterus transplantation. Lancet 2015;385:607–616	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
2. Brännström, et al. One uterus bridging three generations: first live birth after mother-to-daughter uterus transplantation. Fertil Steril 2016;106:261–266	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), ICP, emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
3. Testa, et al. First live birth after uterus transplantation in the United States. Am J Transplant 2018; 18:1270–1274	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
4. Ejzenberg, et al. Livebirth after uterus transplantation from a deceased donor in a recipient with uterine infertility. Lancet 2019;392:2697–2704	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), chorioamnionitis or other infection during or after delivery, emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
5. Brännström, et al. Live birth after robotic-assisted live donor uterus transplantation. Acta Obstet Gynecol Scand 2020;99:1222–1229	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), hemorrhage, emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
6. Brucker, et al. Living-donor uterus transplantation: pre-, intra-, and postoperative parameters relevant to surgical success, pregnancy, and obstetrics with live births. J Clin Med 2020;9:2485	Case series/2	?	?	-	Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), emergency hysterectomy, ICU	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
7. Flyckt, et al. First birth from a deceased donor uterus in the United States: from severe graft rejection to successful cesarean delivery. Am J Obstet Gynecol 2020;223:143–151	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), hemorrhage, emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
8. Huang, et al. Report of the first live birth after uterus transplantation in People's Republic of China. Fertil Steril 2020;114:1108–1115	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
9. Akouri, et al. First live birth after uterus transplantation in the Middle East. Middle East Fertil Soc J 2020;25:30–37	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation

TABLE 2 (Continued)

Number, author	Study design/number of live births	Directness	Study limitations	Precision	Included maternal variables	Included perinatal variables
10. Johannesson, et al. Twelve live births after uterus transplantation in the Dallas UtErus Transplant Study. Obstet Gynecol 2021;137:241–249	Case series/12	?	?	-	Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS)	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar
11. Fronek, et al. Live birth following uterine transplantation from a nulliparous deceased donor. Transplantation 2021;105:1077–1081	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS)	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar
12. Fronek, et al. Human uterus transplantation from living and deceased donors: The interim results of the first 10 cases of the Czech trial. J Clin Med 2021;10:586	Case series/3	?	?/–	-	Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS)	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar
13. Rosenzweig, et al. Pregnancy after CMV infection following uterus transplantation: A case report from the Dallas Uterus Transplant Study. Transpl Infect Dis 2021;23:e13653	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS)	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU
14. Johannesson, et al. Robotic donor hysterectomy results in technical success and live births after uterus transplantation: Subanalysis within the Dallas Uterus Transplant Study (DUETS) clinical trial. Clin Obstet Gynecol 2022;65:59–67	Case series/4	?	?	-	Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS)	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%)
15. Ayoubi, et al. Case report: Post-partum SARS-CoV-2 infection after the first French uterus transplantation. Front Surg 2022;9:854225	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), chorioamnionitis or other infection during or after delivery, ICU, LOHS	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, infection, malformation
16. Ozkan, et al. Birth of a healthy baby 9 years after a surgically successful deceased donor uterus transplant. Ann Surg 2022;275:825–832	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), ICU	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation
17. Schulz, et al. Children after uterus transplantation: 2-year outcomes from the Dallas UtErus Transplant Study (DUETS). BJOG 2022;129:2117–2124	Case series/13	?	+/?	-	Indication for delivery, PROM	Prematurity (gw), el./em. CS, gender, disability/neurodev. delay at 2 years

(Continues)

TABLE 2 (Continued)

Number, author	Study design/number of live births	Directness	Study limitations	Precision	Included maternal variables	Included perinatal variables
18. Brännström, et al. Reproductive, obstetric, and long-term health outcome after uterus transplantation: results of the first clinical trial. Fertil Steril 2022;118:576–585	Case series/9	?	?	-	Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), ICP	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, malformation, disability/ neurodev. delay at 2 years
19. Brucker, et al. Uterine allograft removal by total laparoscopic hysterectomy after successful cesarean delivery in a living-donor uterus recipient with uterovaginal agenesis (MRKHS). Arch Gynecol Obstet 2023;307:827–840	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), ICP, chorioamnionitis or other infection during or after delivery, hemorrhage, emergency hysterectomy, ICU	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU
20. Janota, et al. Three-year follow-up results of two children born from a transplanted uterus. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2023;167:370–375	Case series/2	-	?	-	Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS)	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, infection, malformation, disability/neurodev. delay at 2 years
21. Scollo, et al. Live birth from cryopreserved oocyte after uterus transplantation: a case report. Am J Case Rep 2023;24:e940960	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), chorioamnionitis or other infection during or after delivery, emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight, gender
22. Johannesson, et al. Persistence pays off: live birth after uterus transplant, overcoming recurrent pregnancy loss with cerclage placement. J Clin Med 2023;12:6463	Case report/1				Indication for delivery, PROM, GH, PE, GD, placenta previa/invasive placenta (PAS), chorioamnionitis or other infection during or after delivery, emergency hysterectomy, ICU, LOHS	Prematurity (gw), el./em. CS, weight, gender, Apgar, RDS, PAD, CPAP, respirator, NICU, infection, malformation
23. Ozkan, et al. The Ozkan technique in current use in uterus ransplantation: from the first ever successful attempt to clinical reality. J Clin Med 2023;12:2812	Case series/2	-	?/–	-	Indication for delivery, PROM	Prematurity (gw), el./em. CS, weight, gender, Apgar, NICU, malformation, disability/ neurodev. delay at 2 years
24. York, et al. Neonatal outcomes after uterus transplantation: Dallas Uterus Transplant Study. Am J Perinatol 2023;40:42–50	Case series/12	?	+/?	-	Indication for delivery, PROM, GD	Prematurity (gw), el./em. CS, weight deviation: <10th percentile/<2 SD, weight deviation (%), gender, Apgar, RDS, PAD, CPAP, respirator, NICU, infection, malformation

Abbreviations: CPAP, continuous positive airway pressure; el./em. CS, elective/emergency cesarean section; GD, gestational diabetes; GH, gestational hypertension; gw, gestational week at delivery; ICP, intrahepatic cholestasis of pregnancy; LOHS, length of hospital stay.NICU, neonatal intensive care unit; PAS, placenta accreta spectrum; PE, preeclampsia; PROM, premature rupture of membranes; RDS, respiratory distress syndrome.

TABLE 3 Maternal outcomes of 40 pregnancies leading to live birth after uterus transplantation. Pregnancies with live births are numbered ("indication for delivery" column) center-specific if they are reported in >1 study, as specified in footnotes[a–l] in "women" column. In the included case series (>1 live birth) the live births are tabulated from lowest (top) to highest (bottom) gestational week + days at delivery. All cases have the same respective position in each corresponding case series of Table 3 and Table 4.

Study number, author, journal, year, city, country	Study-design	Women (n)	Indication for delivery	PROM	GH/PH	GD	Placenta previa/PAS	ICP	Chorioamnionitis or other infections during or after delivery	Hemorrhage/ emergency hysterectomy	ICU	LOHS
1. Brännström et al., Lancet 2015, Gothenburg, Sweden	Case report	1[a]	1. PE	No	No/yes	No	No/no	NR	NR	NR/no	No	3d
2. Brännström et al., Fertil Steril 2016, Gothenburg, Sweden	Case report	2[a]	2. ICP	No	No/no	No	No/no	Yes	NR	NR/no	No	8d
3. Testa et al., Am J Transplant 2018, Dallas, USA	Case report	1[b]	3. AKI	No	No/no	No	No/no	NR	NR	NR/no	No	4d
4. Ejzenberg, Lancet 2018, Sao Paulo, Brazil	Case report	1	Elective	No	No/no	No	No/no	NR	Yes	NR/no	No	3d
5. Brännström, Acta Obstet Gynecol Scand 2020, Gothenburg, Sweden	Case report	1	Elective	No	No/no	No	No/no	NR	NR	Yes /no	No	5d
6. Brucker, J Clin Med 2020, Tübingen, Germany	Case series	2	PPROM	Yes	No/no	No	No/no	NR	NR	NR/no	No	NR
			Elective	No	No/no	No	No/no	NR	NR	NR/no		NR
7. Flyckt, Am J Obst Gynecol 2020, Cleveland, USA	Case report	1	Elective	No	No/no	No	Yes/yes	NR	NR	Yes/no	No	4d
8. Huang, Fertil Steril 2020, Xia, China	Case report	1	PTL	No	No/no	No	No/no	NR	NR	NR/no	No	3d
9. Akouri, MEFS J 2020, Beirut, Lebanon	Case report	1	PTL	No	No/no	No	No/no	NR	NR	NR/no	No	4d
10. Johannesson, Obstet Gynecol 2021, Dallas, USA	Case series	11[c]	1. PTL	No	No/no	No	No/no	NR	NR	NR/NR	NR	NR
			2. PTL	No	No/no	No	Yes/no	NR	NR	NR/NR	NR	NR
			3. AKI	No	No/no	No	No/no	NR	NR	NR/NR	NR	NR
			4. PTL	No	No/no	No	No/no	NR	NR	NR/NR	NR	NR
			5. Elective	No	No/no	Yes	No/no	NR	NR	NR/NR	NR	NR
			6. Elective*	No	No/no	No	No/no	NR	NR	NR/NR	NR	NR
			7. Elective	No	No/yes	No	Yes/no	NR	NR	NR/NR	NR	NR
			8. Elective	No	No/no	No	No/no	NR	NR	NR/NR	NR	NR
			9. Elective	No	Yes/no	No	No/no	NR	NR	NR/NR	NR	NR
			10. Elective	No	No/no	No	No/no	NR	NR	NR/NR	NR	NR
			11. Elective	No	No/no	No	No/no	NR	NR	NR/NR	NR	NR
			12. Elective*	No	Yes/no	No	No/no	NR	NR	NR/NR	NR	NR

(Continues)

TABLE 3 (Continued)

Study number, author, journal, year, city, country	Study-design	Women (n)	Indication for delivery	PROM	GH/PH	GD	Placenta previa/PAS	ICP	Chorioamnionitis or other infections during or after delivery	Hemorrhage/ emergency hysterectomy	ICU	LOHS
11. Fronek, Transplantation 2021, Praque, Czech Republic	Case report	1[d]	1. PTL	No	No/no	Yes	No/no	NR	NR	NR/NR	NR	NR
12. Fronek, J Clin Med 2021, Prague, Czech Republic	Case series	3[e]	1. PTL	No	No/no	Yes	No/no	NR	NR	NR/NR	NR	NR
			Elective	No	No/no	Yes	Yes/no	NR	NR	NR/NR	NR	NR
			2. Elective	No	Yes/no	No	No/no	NR	NR	NR/NR	NR	NR
13. Rosenzwieg, Transpl Infect Dis 2021, Dallas, USA	Case report	1[f]	13. PROM	Yes	No/no	No	No/no	NR	NR	NR/NR	NR	3d
14. Johannesson, Clin Obstet Gynecol 2022, Dallas, USA	Case series	4[g]	2. PTL	No	NR/NR	NR	Yes/no	NR	NR	NR/NR	NR	NR
			4. PTL	No	NR/NR	NR	No/no	NR	NR	NR/NR	NR	NR
			9. Elective	No	NR/NR	NR	No/no	NR	NR	NR/NR	NR	NR
			Elective	No	NR/NR	NR	No/no	NR	NR	NR/NR	NR	NR
15. Ayoubi, Front Surg 2022, Paris, France	Case report	1	PE	No	No/yes	No	No/no	NR	Yes	NR/NR	No	48d
16. Ozkan, Ann Surg 2022, Antalya, Turkey	Case report	1	1. PE, FGR	Yes	No/yes	No	No/no	NR	NR	NR/NR	No	NR
17. Schulz, BJOG 2022, Dallas, USA	Case series	13[h]	1. PTL	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			2. PTL	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			3. AKI	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			4. PTL	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			6. Elective*	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			7. Elective	No	NR/yes	NR	NR/NR	NR	NR	NR/NR	NR	NR
			PTL	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			13. PROM	Yes	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			8. Elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			9. Elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			10. Elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			11. Elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			12. Elective*	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR

TABLE 3 (Continued)

Study number, author, journal, year, city, country	Study-design	Women (n)	Indication for delivery	PROM	GH/PH	GD	Placenta previa/PAS	ICP	Chorioamnionitis or other infections during or after delivery	Hemorrhage/ emergency hysterectomy	ICU	LOHS
18. Brännström, Fertil Steril 2022, Gothenburg, Sweden	Case series	6[i]	1. PE	No	No/yes	No	No/no	No	NR	NR/NR	NR	NR
			2. ICP	No	No/no	No	No/no	Yes	NR	NR/NR	NR	NR
			PE, ICP, PPROM	Yes	No/yes	No	No/no	Yes	NR	NR/NR	NR	NR
			Elective*	No	No/no	No	No/no	No	NR	NR/NR	NR	NR
			PE^	No	No/yes	No	No/no	No	NR	NR/NR	NR	NR
			Elective^	No	No/no	No	No/no	No	NR	NR/NR	NR	NR
			Elective*	No	No/no	No	No/no	No	NR	NR/NR	NR	NR
			Elective	No	No/no	No	No/no	No	NR	NR/NR	NR	NR
			Elective	No	No/no	No	No/no	No	NR	NR/NR	NR	NR
19. Brucker, Arch Gynecol Obstet 2023, Tübingen, Germany	Case report	1	AKI	No	No/no	No	No/no	No	Yes	No/no	No	NR
20. Janota, Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2023, Prague, Czech Republic	Case report	2[j]	1. PTL	No	No/no	Yes	No/no	NR	NR	NR/NR	NR	NR
			2. Elective	No	Yes/no	No	Yes/no	NR	NR	NR/NR	NR	NR
21. Scollo, Am J Case Rep 2023, Catania, Italy	Case report	1	PTL	No	No/no	No	NR/NR	NR	Yes	NR/no	Yes	14d
22. Johannesson, J Clin Med 2023, Dallas, USA	Case report	1	Elective	No	No/no	No	No/yes	NR	No	NR/no	No	2d
23. Ozkan, J Clin Med 2023, Antalya, Turkey	Case series	2[k]	1. PE, FGR	Yes	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			PPROM, PTL	Yes	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR

(Continues)

TABLE 3 (Continued)

Study number, author, journal, year, city, country	Study-design	Women (n)	Indication for delivery	PROM	GH/PH	GD	Placenta previa/PAS	ICP	Chorioamnionitis or other infections during or after delivery	Hemorrhage/ emergency hysterectomy	ICU	LOHS
24. York, Obstet Gynecol 2023, Dallas, USA	Case series	11[l]	1. PTL	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			2. PTL	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			3. AKI	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			4. PTL	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			5. Elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			6. Elective*	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			7. Elective	No	NR/NR	Yes	NR/NR	NR	NR	NR/NR	NR	NR
			8. Elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			9. Elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			10.elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			11. Elective	No	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR
			12. elective*	no	NR/NR	NR	NR/NR	NR	NR	NR/NR	NR	NR

Abbreviations: AKI, acute kidney injury, FGR, fetal growth restriction; GD, gestational diabetes, GH, gestational hypertension, ICP, intrahepatic cholestasis of pregnancy, ICU, intensive care unit, LOHS, length of hospital stay, NR, not reported, PAS, placenta spectrum disorder, PE, preeclampsia; PPROM, preterm premature rupture of membranes, PROM, premature rupture of membranes, PTL, preterm labor.

[a]Data also included (with same numbering of case(s)) in study (case series) number 18.

[b]Data also included (with same numbering of case(s)) in studies (case series) numbers 10, 17, 24.

[c]Data also included (with same numbering of case(s)) in studies (case series) numbers 14, 17, 24 and (case report) number 3.

[d]Data also included (with same numbering of case(s)) in study (case series) numbers 12, 20.

[e]Data also included (with same numbering of case(s)) in studies (case series) number 20 and (case report) number 11.

[f]Data also included (with same numbering of case(s)) in study (case series) number 17.

[g]Data also included (with same numbering of case(s)) in studies (case series) numbers 10, 17, 24.

[h]Data also included (with same numbering of case(s)) in studies (case series) numbers 10, 14, 24 and (case report) numbers 3, 13.

[i]Data also included (with same numbering of case(s)) in studies (case reports) numbers 1, 2.

[j]Data also included (with same numbering of case(s)) in studies (case series) number 12 and (case report) number 11.

[k]Data also included (with same numbering of case(s)) in study (case report) number 16.

[l]Data also included (with same numbering of case(s)) in studies (case series) numbers 10, 14, 17 and (case report) number 3.

*,^Pregnancies with two live births from same mother within specific case series.

TABLE 4 Perinatal outcomes of 40 live births after uterus transplantation. Live births are numbered ("prematurity (gw)" column) center-specific if they are reported in >1 study, as specified in footnotes [a-l] in "children" column. In the included case series (>1 live birth) the live births are tabulated from lowest (top) to highest (bottom) gestational week + days at delivery. All cases have the same respective position in each corresponding case series of Table 3 and Table 4.

Study number, author, journal year, city, country	Study design	Children (n)	Prematurity (gw)	Elective/ emergency CS	10th pc. / <2 SD, weight deviation (%)	Weight (g)	Gender	Apgar <5 at 5 min. (1, 5, 10 min.)	RDS/PAD	CPAP/ respirator	NICU	Infection	Malformation	Disability/ neurodev. delay at 2 years
1. Brännström et al., Lancet 2015, Göteborg, Sweden	Case report	1[a]	1.Yes (31+6)	Emergency	(−9%)	1775	M	No (9, 10, 10)	Yes/no	Yes/no	16d	NR	No	NR
2. Brännström et al., Fertil Steril 2016, Gothenburg, Sweden	Case report	1[a]	2.Yes (34+4)	Emergency	(−7%)	2335	M	No (9, 10, 10)	Yes/no	Yes/no	2d	NR	No	NR
3. Testa et al., Am J Transplant 2018, Dallas, USA	Case report	1[b]	3.Yes (33+1)	Emergency	(+10%)	1995	M	No (8, 9, NR)	No/no	No/no	No	NR	No	NR
4. Ejzenberg, Lancet 2018, Sao Paulo, Brazil	Case report	1	Yes (35+3)	Elective	(−5%)	2550	F	No (9, 10, 10)	No/no	No/no	No	NR	No	NR
5. Brännström, Acta Obstet Gynecol Scand 2020, Gothenburg, Sweden	Case report	1	Yes (36+1)	Elective	(+3%)	2894	M	No (9, 10, 10)	No/no	No/no	No	NR	No	NR
6. Brucker, J Clin Med 2020, Tübingen, Germany	Case series	2	Yes (35+1)	Emergency	<10th pc. (−17%)	2180	M	No (9, 10,10)	No/no	No/no	No	NR	No	NR
			Yes (36+3)	Elective	(−13%)	2500	M	No (8, 8, 8)	Yes/no	Yes/no	3d	NR	No	NR
7. Flyckt, Am J Obst Gynecol 2020, Cleveland, USA	Case report	1	Yes (34+2)	Elective	<10th pc. (−21%)	1930	NR	No (8, 9, NR)	No/no	No/no	No	NR	No	NR
8. Huang, Fertil Steril 2020, Xia, China	Case report	1	Yes (33+6)	Emergency	(−15%)	2000	M	No (10, 10, 10)	No/no	No/no	No	NR	No	NR
9. Akouri, MEFS J 2020, Beirut, Lebanon	Case report	1	Yes (35+1)	Emergency	(+/−0%)	2620	F	No (9, 10, 10)	No/no	No/no	No	NR	No	NR
10. Johannesson, Obstet Gynecol 2021, Dallas, USA	Case series	12[c]	1.Yes (30+6)	Emergency	(+/−0%)	1770	F	No (7, 8, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			2.Yes (32+4)	Emergency	(+12%)	2350	M	No (7, 8, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			3.Yes (33+1)	Emergency	(+10%)	1995	M	No (8, 9, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			4.Yes (35+5/6[§])	Emergency	(−15%)	2325	F	No (8, 8, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			5.Yes (35+6)	Elective	(+4%)	2860	F	No (8, 8, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			6.Yes (36+6)	Elective*	(−2%)	2920	F	No (9, 9, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			7.Yes (36+6)	Elective	<10th pc. (−19%)	2400	F	No (8, 9, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			8.no (37+0)	Elective	(−1%)	2960	M	No (8, 9, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			9.no (37+0)	Elective	(+1%)	3025	M	No (4, 8/9[§], NR)	NR/NR	NR/NR	NR	NR	NR	NR
			10.no (37+2)	Elective	(+3%)	3140	M	No (8, 8, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			11.no (38+0)	Elective	(+5%)	3370	F	No (9, 9, NR)	NR/NR	NR/NR	NR	NR	NR	NR
			12.no (38+0)	Elective*	(+9%)	3470	F	No (9, 9, NR)	NR/NR	NR/NR	NR	NR	NR	NR

(Continues)

TABLE 4 (Continued)

Study number, author, journal year, city, country	Study design	Children (n)	Prematurity (gw)	Elective/ emergency CS	10th pc. / <2 SD, weight deviation (%)	Weight (g)	Gender	Apgar <5 at 5 min. (1, 5, 10 min.)	RDS/PAD	CPAP/ respirator	NICU	Infection	Malformation	Disability/ neurodev. delay at 2 years
11. Fronek, Transplantation 2021, Prague Czech Republic	Case report	1[d]	1.Yes (34+6)	Emergency	(+7%)	2735	M	No (7, 9, 9)	NR/NR	NR/NR	NR	NR	NR	NR
12. Fronek, J Clin Med 2021, Prague Czech Republic	Case series	3[e]	1. Yes (34+6)	Emergency	(+7%)	2735	M	No (7, 9, 9)	NR/NR	NR/NR	NR	NR	NR	NR
			Yes (35+3)	Elective	<10th pc. (-21%)	2115	F	No (9, 10, 10)	NR/NR	NR/NR	NR	NR	NR	NR
			2. Yes (36+2)	Elective	<10th pc. (−19%)	2300	F	No (10, 10, 10)	NR/NR	NR/NR	NR	NR	NR	NR
13. Rosenzweig, Transpl Infect Dis 2021, Dallas, USA	Case report	1[f]	13. No (37+0)	Emergency	(+8%)	3220	M	No (8, 9, NR)	No/no	No/no	No	NR	NR	NR
14. Johannesson, Clin Obstet Gynecol 2022, Dallas, USA	Case series	4[g]	2. Yes (32+4)	Emergency	(+12%)	2350	NR	NR	NR/NR	NR/NR	NR	NR	NR	NR
			4. Yes (35+5/6[§])	Emergency	(−15%)	2325	NR	NR	NR/NR	NR/NR	NR	NR	NR	NR
			No (37+0)	Elective	(+1%)	3025	NR	NR	NR/NR	NR/NR	NR	NR	NR	NR
			No (37+0)	Elective	(+10%)	3220	NR	NR	NR/NR	NR/NR	NR	NR	NR	NR
15. Ayoubi, Front Surg 2022, Paris, France	Case report	1	Yes (32+4)	Emergency	(+8%)	1845	F	No (7, 8, 10)	No/no	No/no	No	Yes	No	NR
16. Ozkan, Ann Surg 2022, Antalya, Turkey	Case report	1	1.Yes (28+4)	Emergency	<10th pc. / <2 SD (−39%)	760	M	No (7, 8, 8)	Yes/no	Yes/no	79d	NR	No	NR
17. Schulz, BJOG 2022, Dallas, USA	Case series	13[h]	1. Yes (30+6)	Emergency	NR	NR	F	NR	NR	NR/NR	NR	NR	NR	No
			2. Yes (32+4)	Emergency	NR	NR	M	NR	NR	NR/NR	NR	NR	NR	NR
			3. Yes (33+1)	Emergency	NR	NR	M	NR	NR	NR/NR	NR	NR	NR	No
			4. Yes (35+5/6[§])	Emergency	NR	NR	F	NR	NR	NR/NR	NR	NR	NR	NR
			6. Yes (36+6)	Elective	NR	NR	F	NR	NR	NR/NR	NR	NR	NR	No
			7. Yes (36+6)	Elective	NR	NR	F	NR	NR	NR/NR	NR	NR	NR	NR
			Yes (36+6)	Emergency	NR	NR	F	NR	NR	NR/NR	NR	NR	NR	NR
			13. No (37+0)	Emergency	NR	NR	M	NR	NR	NR/NR	NR	NR	NR	NR
			8. No (37+0)	Elective	NR	NR	M	NR	NR	NR/NR	NR	NR	NR	No
			9. No (37+0)	Elective	NR	NR	M	NR	NR	NR/NR	NR	NR	NR	NR
			10. No (37+2)	Elective	NR	NR	M	NR	NR	NR/NR	NR	NR	NR	Yes
			11. No (38+0)	Elective	NR	NR	F	NR	NR	NR/NR	NR	NR	NR	NR
			12. No (38+0)	Elective	NR	NR	F	NR	NR	NR/NR	NR	NR	NR	NR

TABLE 4 (Continued)

Study number, author, journal year, city, country	Study design	Children (n)	Prematurity (gw)	Elective/ emergency CS	10th pc. / <2 SD, weight deviation (%)	Weight (g)	Gender	Apgar <5 at 5 min. (1, 5, 10 min.)	RDS/PAD	CPAP/ respirator	NICU	Infection	Malformation	Disability/ neurodev. delay at 2 years
18. Brännström, Fertil Steril 2022, Gothenburg, Sweden	Case series	9[i]	1. Yes (31+6)	Emergency	(−9%)	1775	M	No (9, 10, 10)	Yes/no	Yes/no	16d	NR	No	No
			2. Yes (34+4)	Emergency	(−7%)	2335	M	No (9, 10, 10)	Yes/no	Yes/no	5d	NR	No	No
			Yes (34+4)	Emergency	(+23%)	3074	M	No (3, 7, 10)	Yes/no	Yes/no	No	NR	No	No
			Yes (35+0)	Elective*	(+4%)	2700	M	No (8, 8, 8)	Yes/no	Yes/no	7d	NR	No	No
			Yes (35+3)	Emergency^	(−4%)	2552	F	No (9, 10, 10)	No/no	No/no	No	NR	No	No
			Yes (35+6)	Elective^	(−1%)	2745	M	No (9, 10, 10)	No/no	No/no	2d	NR	No	No
			No (37+0)	Elective*	(−13%)	2600	F	No (9, 10, 10)	No/no	No/no	No	NR	No	No
			No (37+1)	Elective	(−12%)	2676	F	No (9, 10, 10)	No/no	No/no	No	NR	No	No
			No (38+0)	Elective	(−4%)	3078	F	No (9, 10, 10)	No/no	No/no	No	NR	No	No
19. Brucker, Arch Gynecol Obstet 2023, Tübingen, Germany	Case report	1	Yes (33+4)	Emergency	<10th pc. / <2 SD (-29%)	1635	M	No (8, 9, 9)	Yes/no	Yes/no	1d	NR	NR	NR
20. Janota, Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2023, Prague, Czech Republic	Case report	2[j]	1. Yes (34+6)	Emergency	(+7%)	2735	M	No (7, 9, 9, 9)	Yes/no	Yes/no	2d	No	No	No
			2. Yes (36+2)	Elective	<10th pc. (−19%)	2300	F	No (10, 10, 10)	No/no	No/no	No	No	No	No
21. Scollo, Am J Case Rep 2023, Catania, Italy	Case report	1	Yes (34+0)	Emergency	<10th pc. / <2 SD (-28%)	1725	F	NR	NR/NR	NR/NR	NR	NR	NR	NR
22. Johannesson, J Clin Med 2023, Dallas, USA	Case report	1	No (37+6)	Elective	(−9%)	2880	F	No (8, 9, NR)	No/no	No/no	No	No	No	NR
23. Ozkan, J Clin Med 2023, Antalya, Turkey	Case series	2[k]	1.(28+)	Emergency	<10th pc. / <2 SD (-39%)	760	M	No (7, 8, 8)	NR/NR	NR/NR	79d	NR	No	No
			(28+)	Emergency	(+21%)	1720	F	No (7, 8, 8)	NR/NR	NR/NR	47d	NR	No	NR

(Continues)

TABLE 4 (Continued)

Study number, author, journal year, city, country	Study design	Children (n)	Prematurity (gw)	Elective/ emergency CS	10th pc. / <2 SD, weight deviation (%)	Weight (g)	Gender	Apgar <5 at 5 min. (1, 5, 10 min.)	RDS/PAD	CPAP/ respirator	NICU	Infection	Malformation	Disability/ neurodev. delay at 2 years
24. York, Am J Perinatol 2023, Dallas, USA	Case series	12[l]	1. Yes (30+6)	Emergency	(+/−0%)	1770	F	No (7, 8, NR)	Yes/no	Yes/no	3d	Yes	No	NR
			2. Yes (32+4)	Emergency	(+12%)	2350	M	No (7, 8, NR)	Yes/no	Yes/no	2d	No	No	NR
			3. Yes (33+1)	Emergency	(+10%)	1995	M	No (8, 9, NR)	Yes/no	Yes/no	4d	Yes	No	NR
			4. Yes (35+5/6[§])	Emergency	(−15%)	2325	F	No (8, 8, NR)	Yes/no	No/no	2d	No	No	NR
			5. Yes (35+6)	Elective	(+4%)	2860	F	No (8, 8, NR)	Yes/no	Yes/no	3d	No	No	NR
			6. Yes (36+6)	Elective*	(−2%)	2920	F	No (9, 9, NR)	No/no	No/no	No	No	Yes	NR
			7. Yes (36+6)	Elective	<10th pc. (−19%)	2400	F	No (8, 9, NR)	No/no	No/no	No	No	No	NR
			8. No (37+0)	Elective	(−1%)	2960	M	No (8, 9, NR)	No/no	No/no	2d	No	No	NR
			9. No (37+0)	Elective	(+1%)	3025	M	No (4, 8/9[§], NR)	Yes/no	Yes/no	1d	No	No	NR
			10. No (37+2)	Elective	(+3%)	3140	M	No (8, 8, NR)	No/no	No/no	2d	No	No	NR
			11. No (38+0)	Elective	(+5%)	3370	F	No (9, 9, NR)	No/no	No/no	No	No	No	NR
			12. No (38+0)	Elective*	(+9%)	3470	F	No (9, 9, NR)	No/no	No/no	No	No	No	NR

Abbeviations: CS, Cesarean section, CPAP, continuous positive airway pressure, F, female, M, male, gw, gestational week at delivery, NICU, neonatal intensive care unit, NR, not reported, PAD, pulmonary adaption disorder, RDS, respiratory distress syndrome, pc, percentile, SD, standard deviation.

[a]Data also included (with same numbering of case(s)) in study (case series) number 18.

[b]Data also included (with same numbering of case(s)) in studies (case series) numbers 10, 17, 24.

[c]Data also included (with same numbering of case(s)) in studies (case series) numbers 14, 17, 24 and (case report) number 3.

[d]Data also included (with same numbering of case(s)) in study (case series) numbers 12, 20.

[e]data also included (with same numbering of case(s)) in studies (case series) number 20 and (case report) number 11.

[f]Data also included (with same numbering of case(s)) in study (case series) number 17.

[g]Data also included (with same numbering of case(s)) in studies (case series) numbers 10, 17, 24.

[h]Data also included (with same numbering of case(s)) in studies (case series) numbers 10, 14, 24 and (case report) number 3.

[i]Data also included (with same numbering of case(s)) in studies (case reports) numbers 1, 2.

[j]Data also included (with same numbering of case(s)) in studies (case series) number 12 and (case report) number 11.

[k]Data also included (with same numbering of case(s)) in study (case report) number 16.

[l]Data also included (with same numbering of case(s)) in studies (case series) numbers 10, 14, 17 and (case report) number 3.

*,^Live birth from same mother within specific case series.

[§]=gw reported differently in studies (case series) numbers 10, 14, 17, 24.

TABLE 5 Summary of rates (%) of maternal and perinatal complications among singleton pregnancies with live births (n=40) after uterus transplantation.

Maternal outcomes		Perinatal outcomes	
Gestational hypertension	7.5%	Prematurity	70.0%
Preeclampsia	15.0%	Respiratory distress syndrome	35.0%
Premature rupture of membranes	15.0%	CPAP treatment	32.5%
Placenta previa	10.0%	Weight deviation <10th percentile	20.0%
Gestational diabetes	7.5%	Weight deviation <2 SD percentile	7.5%
Placenta accreta spectrum	5.0%	Congenital malformation	2.5%
Intrahepatic cholestasis of pregnancy	5.0%		

Abbreviations: CPAP, continuous positive airway pressure, SD, standard deviation.

There were no reported events of the outcome Apgar score <5 at 5 min, but since Apgar scores at 1 and 5 min were reported for all live births, with Apgar at 10 min values also reported in some cases, we have included Apgar data in Table 4.

The rates of birthweight <10th percentile and <2 SD were in 8/40 (20.0%) and 3/40 (7.5%) neonates, respectively. Respiratory distress syndrome was reported in 14/40 (35.0%) and 13 of these infants were on CPAP. Care in neonatal intensive care unit (NICU) was needed for 16 infants, with the median time in NICU being 2.5 days (range one to 79 days) and with NICU for more than 1 week only needed for three very preterm infants (one born at gestational week 31 who stayed for 16 days in NICU, and two neonates born at gestational week 28 stayed for 47 and 79 days respectively in NICU).

One case of minor congenital malformation (displaced urethra in female infant) was reported. Of the 17 children who had completed follow-up for 2 years, one had neurodevelopmental disability. None of the studies reported outcomes of need for respirator, hypoxic ischemic encephalopathy, need for therapeutic hypothermia/seizures, meconium aspiration syndrome, or perinatal mortality.

3.3 | Summary of major maternal and perinatal outcomes

A summary of rates of specific maternal and perinatal outcomes with comparatively high rates are shown in Table 5.

4 | DISCUSSION

It is important to assess the safety and efficacy of any new interventional procedure in clinical medicine. UTx is a novel infertility treatment which offers hope for women with AUFI, who previously were untreatable. This systematic review comprising data from 40 live births from 36 women, as documented in either case reports or case series, illustrates an increased risk for both mothers and infants in pregnancies following UTx. It is not surprising that the initial births after UTx were published in the format of case reports since these reports contained rather novel data, such as those of the first live births after live donor UTx and deceased donor UTx, both covered in comprehensive articles in the Lancet.[1,3] We were not able to find any data from studies of a higher evidence grade than case series, such as controlled prospective studies.

GH complicated 7.5% of pregnancies, whereas 15.0% were affected by PE. Comparatively, the annual report from the Swedish Pregnancy Register published in 2021, covering 107 419 number of births, revealed a PE incidence of 5.9% among primiparous women.[34] The increased risk of GH/PE could partly be related to the well-described nephrotoxic effect of tacrolimus, which is used as the principal IS after UTx.[35] In our present study we also identified that the risk of placenta previa and PAS is high and equates to the risk following three previous cesarean sections.[36] The incidence of ICP varies across different parts of the world, ranging from 0.1% to 2%, while the condition itself carries a 3.5-fold increased risk of preterm birth.[37] In the present study, two pregnancies (5.0%) were affected by ICP, which is notably high and could contribute to the increased risk of preterm birth. The standard IS treatment in pregnancies after UTx is tacrolimus, steroids plus azathioprine and it may well be that the azathioprine component contributes to the high ICP rate, in line with findings from an earlier study of women with azathioprine treatment of inflammatory bowel disease during pregnancy.[38] Other factors contributing to preterm birth include the increased risk of PE and GH, as well as PROM, the latter affecting 15% as compared to the described overall rate in the general population of pregnancies leading to childbirth of 1%–3% for PROM.[39] It should be emphasized that 47.5% of deliveries were unplanned emergency cesarean sections due to maternal or obstetrical complications, and this is evidently a very high rate. In comparison, between 9.6% and 21% underwent emergency cesarean sections after one previous cesarean section in the eastern part of Sweden in 2018.[40] However, we caution readers that total number of pregnancies is very small and change in numerator by one or two will have significant influence on these estimates.

We did not identify any comparable group of women undergoing an alternative infertility treatment with similar characteristics to those undergoing pregnancy after UTx. However, reasonable comparative groups could be pregnancies in women with solid organ transplantations, such as kidney, liver, and heart, and women undergoing IVF

pregnancies with donated oocytes, where the fetus is fully allogenic to the uterus, similarly to after UTx. Pregnancies following solid organ transplantation have shown increased frequencies of both PE (20%–50%), PTL (40%–90%), gestational diabetes (2.5%–5.1%), and fetal growth restriction (16%–21.2%).[6,41–45] However, this comparison is also flawed as these transplanted women, as a group, are likely to be of less general health than those who have undergone UTx. Pregnancies following oocyte donation also demonstrate increased risks, ranging from 9.3%–16.9% for PE and up to 13% for gestational diabetes.[46]

All births included in this review took place by cesarean section, which is unsurprising given the novelty of the procedure, the fact that the vast majority of the mothers have MRKHs and have undergone neovagina surgery or vaginal dilation prior to transplantation, that a fibrotic stenosis is typically seen at the vaginal-vaginal anastomosis site, and that it is unclear how the contraction pattern would manifest in a transplanted uterus.

The result of the present systematic review shows that the rate of preterm births was as high as 70.0%, but that 52.4% of elective cesarean sections were provider-initiated and scheduled prior to 37 completed gestational weeks. Our own experience in this field is that the initial births of the first clinical trial were planned just after completion of 35 gestational weeks, as a compromise between fetal maturity and risk of adverse obstetric events during the last weeks of pregnancy. The rate of respiratory distress syndrome in these initial elective deliveries was very high and we modified the local recommendations to aim for elective birth at 37+ gestational weeks. At Sahlgrenska University Hospital, 3% of babies born vaginally in an obstetric low-risk group (Robson 1, denoting cephalic position after a healthy pregnancy from a healthy nulliparous mother with spontaneously initiated contractions) are admitted to NICU. This rate is comparable with the suggested 10% standard for neonatal healthcare needs in a Swedish delivery ward.[47] This obviously differs significantly from the figures observed among the 40 children of the present study where, for example, CPAP treatment was deemed necessary in 32.5%. It is possible that this rate could be lowered considerably with more experience and by attempting to postpone the delivery time as far as the condition of the child and the mother allows. Fetal growth restriction (<10 percentile according to Marsal et al.[10]) was described in 20% of cases, which is 2.5-fold higher than the 7.8% described in the general population.[48] Furthermore, congenital malformation was described in one case (2.5%). Malformations are typically found in approximately 2%–4% of live births in the general population,[49] but naturally the fact that the result of the present study is based on very few observations precludes any further comparative analysis.

One important fact to bear in mind is that pregnancy after UTx can only occur after assisted reproduction by IVF, since the oviducts are not included in the graft and natural conception can thereby not occur. Assisted reproduction by IVF with ET is associated with a higher risk for certain perinatal and maternal complications and such information must be considered when discussing the results of the present study. Of note is that the first human UTx procedure in the world, performed in 2000, was carried out with the inclusion of oviducts in the graft but no pregnancy attempts were made before transplantectomy 3 months after UTx.[9]

Another consideration regarding scientific publications in a new field such as UTx is that when novel procedures by geographical location and methodology have been published it will be difficult to publish results of case reports and smaller case series, which would confirm the already known main results. Thus, the UTx field must rely on future data being presented as multi-center collective data accumulation and data from the ongoing international UTx registry, with the first report containing information from 19 live births.[50] However, data collected into that registry only covers a minor part of the outcomes of the present study and the follow-up of children is currently non-existent. We have initiated discussions with several international teams around the creation of a UTx-pregnancy and child registry. This registry would cover data from pregnancy through delivery and the neonatal period, and extend into early adulthood.

5 | CONCLUSION

This systematic review reports perinatal and maternal complications in the context of UTx. Given the treatment's infancy and the inclusion of mainly case reports and series, resulting in a very low certainty of evidence, continuous follow-up and dissemination of data are imperative. This underscores the need for advancements and modifications of the procedure, such as robotic surgery in UTx, to be comprehensively reported. Our study further emphasizes the significance of early detection of conditions like PE and PTL during monitoring. Additionally, it highlights the increased risk of placenta previa and PAS at delivery, emphasizing the importance of optimal timing for delivery.

AUTHOR CONTRIBUTIONS

Mats Brännström, Hans Bokström and Ylva Carlsson contributed equally to study set-up, selection process, assessment of articles, extraction of data, interpretation of data, and writing of manuscript. Henrik Hagberg contributed to study set-up, interpretation of data, and the writing of the manuscript. All authors have read and approved the final version for publication.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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