

Pregnancy and Transplant

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Disclosures

 **I have no relevant financial disclosures**

Background

The first known post-transplant pregnancy occurred in 1958 in a female recipient who had received a kidney from her identical twin sister.



Background


She had 2 live births and her donor had 4 live births.



Background



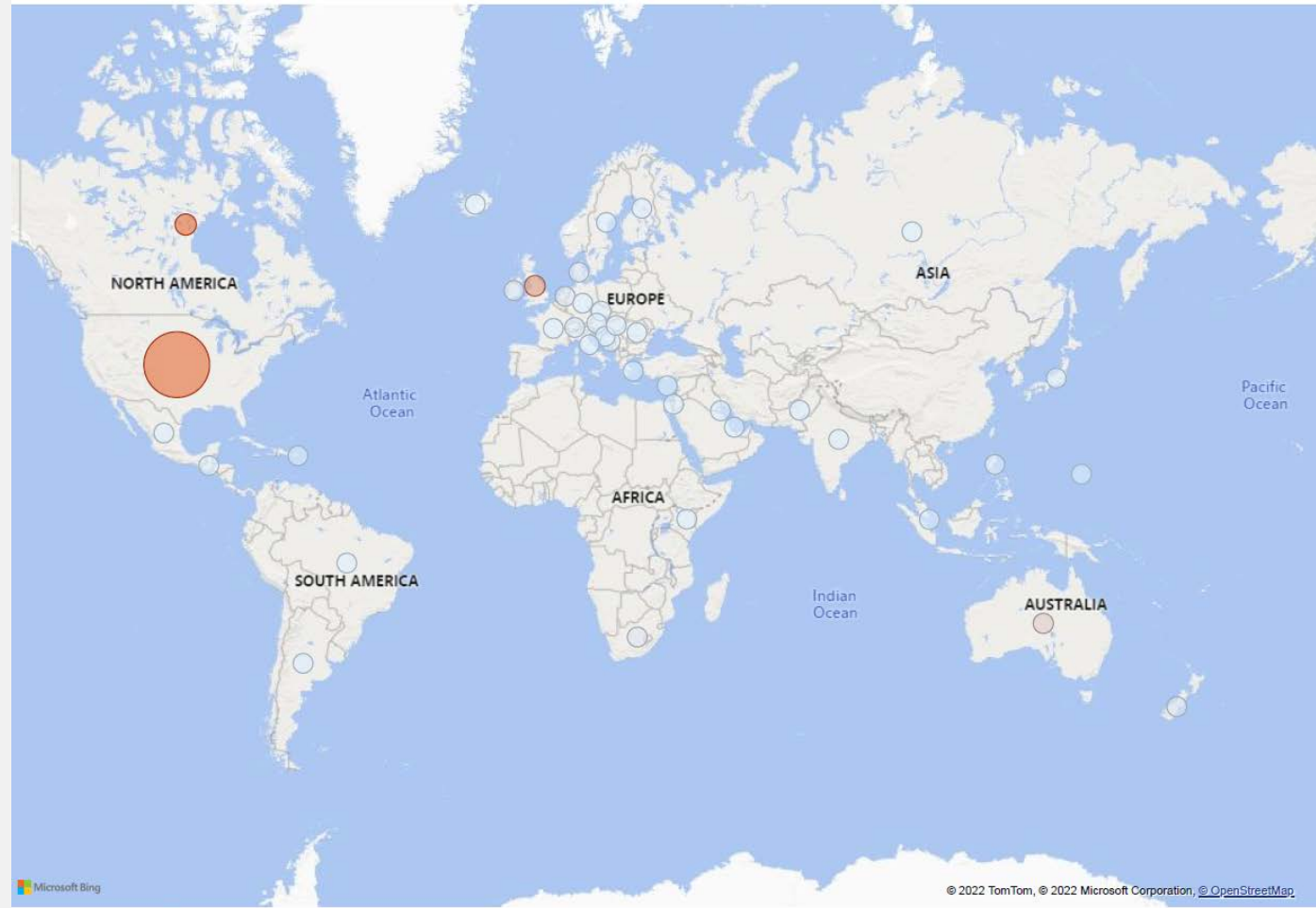
The Transplant Pregnancy Registry International (TPRI) is a voluntary pregnancy registry which has been collecting pregnancy information for over 30 years.

-  **The TPRI uses a simple method for data collection which includes:**
 - informed consent**
 - telephone interview with the participant**
 - medical records review and interviews with healthcare providers**
 - long-term follow-up interviews to monitor recipient and offspring health**

3,039 TPRI TOTAL RECIPIENTS

8/31/22

Country	N
USA/Puerto Rico	2796
Canada	93
UK	58
Australia	25
South Africa	7
Netherlands	6
New Zealand	6
Ireland	5
Denmark	5
Philippines	3
Argentina	2
Czech Republic	2
Finland	2
India	2
Mexico	2
Sweden	2
Switzerland	2
Austria, Bosnia and Herzegovina, Brazil, Croatia, Cyprus, France, Greece, Guam, Guatemala, Hungary, Iceland, Israel, Italy, Japan, Kenya, Kuwait, Qatar, Pakistan, Romania, Russia, Singapore	1 each



TPRI: Pregnancy Outcomes in Female Transplant Recipients



Organ	Recipients	Pregnancies	Outcomes
Kidney	1,279	2,270	2,357
Liver	366	724	743
Liver-Kidney	13	21	22
Liver-Lung	1	1	1
Intestine	2	3	3
Kidney-Pancreas	72	132	140
Pancreas alone	7	16	16
Uterus	3	3	3
Heart	111	190	195
Heart-Kidney	1	1	1
Heart-Lung	6	6	6
Lung	44	57	59
Heart-Liver	1	2	2
Heart-Lung-Liver	1	1	1
Heart-Lung-Kidney	1	2	2
Totals	1,909	3,433	3,555

TPRI: Pregnancies Fathered by Male Transplant Recipients



Organ	Recipients	Fathered Pregnancies	Outcomes
Kidney	637	1,000	1,022
Liver	90	154	161
Liver-Kidney	4	8	8
Liver-Heart-Kidney	1	2	2
Multi-visceral	5	16	16
Pancreas-Kidney	34	43	45
Heart	123	185	191
Heart-Lung-Kidney	1	3	3
Lung	8	10	11
Totals	901	1,413	1,451

Released December 2006
Revised March 2012
Reviewed May 2015
Reviewed April 2017

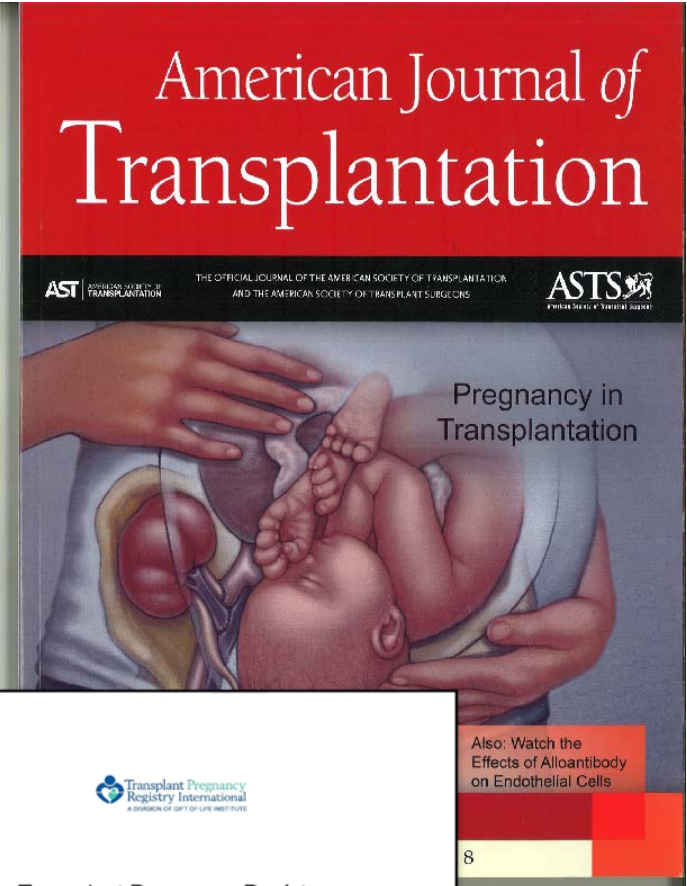
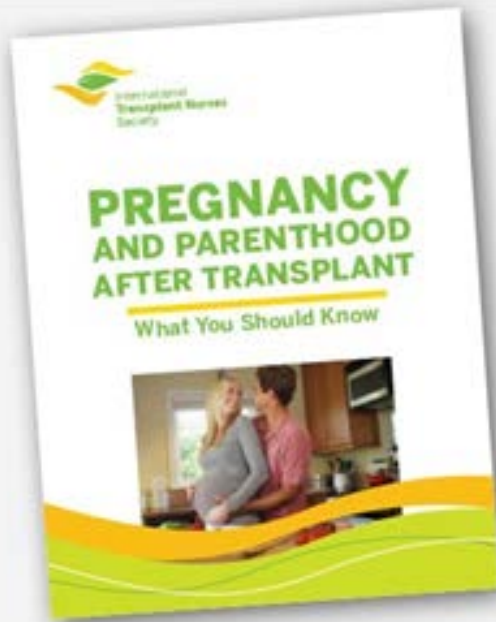
Being a Parent After Receiving a New Transplant

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Also: Watch the
Effects of Alloantibody
on Endothelial Cells

8



Transplant Pregnancy Registry International *(Formerly National Transplantation Pregnancy Registry)*

2020 Annual Report

Issued October 23, 2021

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Pre-pregnancy Recommendations

AST Consensus Statement (2005):

-  **good general health for at least 1 year since transplant**
-  **minimal immunosuppression**
-  **lower risk of infectious complications**
-  **allow sufficient time for stable graft function**
-  **no rejection in the last year prior to pregnancy**
-  **no high blood pressure or well-controlled high blood pressure (with medication safe for pregnancy)**
-  **no or minimal protein in the urine**

Maintenance Immunosuppression

- ❖ **Generally considered “safe”**
 - **cyclosporine, tacrolimus, prednisone, azathioprine**
- ❖ **Contraindicated during pregnancy**
 - **Mycophenolate mofetil, mycophenolic acid (MPA)**
- ❖ **Not enough information**
 - **belatacept, sirolimus, everolimus**

Maintenance Immunosuppression



- ❖ **In 2007 the FDA changed the pregnancy category for MPA based on TPRI data and additional information from the medical literature and the manufacturer.**
- ❖ **This medication was given a warning that pregnancy should not occur while on this medication.**

Pregnancy Outcomes in Female Transplant Recipients with MPA Exposure



- ❖ 152 conceptions in female recipients with exposure to mycophenolic acid products (MPA)
 - 78 (51%) live births
 - 70 (46%) miscarriages
 - 3 stillbirths
 - 1 terminations
- ❖ Of the 78 live births, 14 had birth defects (18%)

Pregnancy Outcomes in Female Transplant Recipients with MPA Exposure

MPA phenotype



Perez-Aytes et al., Am J Med Genet Part A 2008;146A:1-7

Jackson P et al. Am J Med Genet Part A 2009; 149A(6): 1231-1236

Everolimus/Sirolimus

Pregnancy outcomes with exposure to sirolimus or everolimus (no concomitant MPA exposure)

	Sirolimus	Everolimus
Recipients	37	5
Pregnancies	47	6
Outcomes	49	7
Concomitant CSA/tac exposure	43	6
Stillbirth	1 (2%)	0
Terminations	2 (4%)	0
Miscarriages	11 (23%)	2 (29%)
Live births	33 (70%)¹	5 (71%)²

¹Birth defects: Tetralogy of Fallot and vermian hypoplasia of the cerebellum

²cystic hygroma

- ❖ **4 kidney, 7 pregnancies**
- ❖ **4 live births and 3 miscarriages**
 - ❖ **Two miscarriages were unplanned and had exposure to MPA; one live birth had MPA exposure**
- ❖ **The 4 children exposed to belatacept were all reported healthy and developing well with a follow-up of a few months up to 2 years old.**
 - ❖ **There were no birth defects reported in the newborn**
- ❖ **Additional report in the literature of belatacept exposure:**
 - ❖ **liver recipient resulted in a live birth with no birth defects**
 - ❖ **The infant had normal growth and development at 1 year follow-up**

Summary: Medications

- ❖ **Overall, there is not one medication regimen recommended over another, except with MPA.**
- ❖ **Currently, with limited belatacept experience and the product labeling and most common regimen including MPA, assessment of pregnancy safety is unclear.**
- ❖ **To date, sirolimus exposure during pregnancy does not appear to be associated with a pattern of birth defects or problems associated with the fetus.**
- ❖ **Data are limited regarding everolimus exposure during pregnancy.**

Abdominal organ recipients: Maternal outcomes

	Kidney	Liver	Kidney-Pancreas
Recipients	1251	363	71
Pregnancies	2233	716	131
Est conception range	July 1967- Oct 2020	Nov 1985 - July 2020	June 1989 - July 2019
Age at 1st transplant (yrs)	24	20	29.4
Transplant-to-conception (yrs)	5.4	8.9	4.4
Unplanned pregnancy	30%	36%	36%
During pregnancy			
Hypertension	48%	21%	50%
Diabetes	8%	8%	2%
Preeclampsia	29%	21%	34%
Rejection*	3%	5%	5%
After pregnancy			
Graft loss in 2 yrs of delivery	5.4%	2.5%	11%

*any type of rejection-chronic or acute








Moritz, Constantinescu, Coscia et al. TPRI, 2020 Annual Report

Abdominal organ recipients: Newborn outcomes

	Kidney	Liver	Kidney- Pancreas
Pregnancy Outcomes*	2318	734	139
Live Births	1735 (75%)	528 (72%)	94 (68%)
Gestational age	35.8 wks	36.7 wks	34.1 wks
Late preterm (32-<37 wks)	37%	26%	51%
Very preterm (28<32 wks)	6%	5%	14%
Birth weight	2555 g	2772 g	2142 g
Low birth weight (<2500 g)	42%	28%	62%
Cesarean section	50%	42%	68%
Birth defects	4.6%	5.5%	2.1%
Neonatal deaths (within 30 days of birth)	1%	1%	1%

* includes multiple births

Summary-Kidney Recipients

-  **Deliver one month early**
-  **50% of babies are premature**
-  **The mean birth weight ~ 2500g (approximately 5 ½ pounds)**
-  **High risk of HTN and preeclampsia**
-  **Preeclampsia may be difficult to diagnose**
-  **UTI's are common**
-  **Minor increase in serum creatinine may signal rejection**

Thoracic organ recipients: Maternal outcomes

	Heart	Lung
Recipients	110	41
Pregnancy outcomes (includes multiples)	187	54
Age at 1st transplant (yrs)	20	27
Transplant-to-conception (yrs)	7.7	4.1
Unplanned	37%	54%
During pregnancy		
Hypertension	48%	59%
Diabetes	8%	30%
Preeclampsia	27%	15%
Rejection*	8%	13%
After pregnancy		
Graft loss within 2 yrs of delivery	2.7%	5.6%






*biopsy-proven rejection

Thoracic organ recipients: Newborn outcomes








	Heart	Lung
Pregnancy Outcomes*	177	50
Live Births	131 (68%)	35 (63%)
Gestational age	36.2 wks	34.0 wks
Late Preterm (32 to <37wks)	32%	34%
Very Preterm (28- <32 wks)	5%	20%
Birth weight	2595 g	2192 g
Low birth weight (<2500 g)	37%	66%
Cesarean section	45%	47%
Birth defects	8.4%	8.6%
Neonatal deaths (within 30 days of birth)	0	9%

* includes multiple births

Summary-Heart Recipients

-  **Female heart transplant recipients are able to maintain a pregnancy with the majority resulting in a live birth**
-  **Preterm and low birth weight infants are common (~50%)**
-  **Pre-pregnancy counseling should include 2 specific topics:**
 -  **Potentially inheritable cardiomyopathies**
 -  **Maternal survival unrelated to pregnancy**

Summary-Lung Recipients

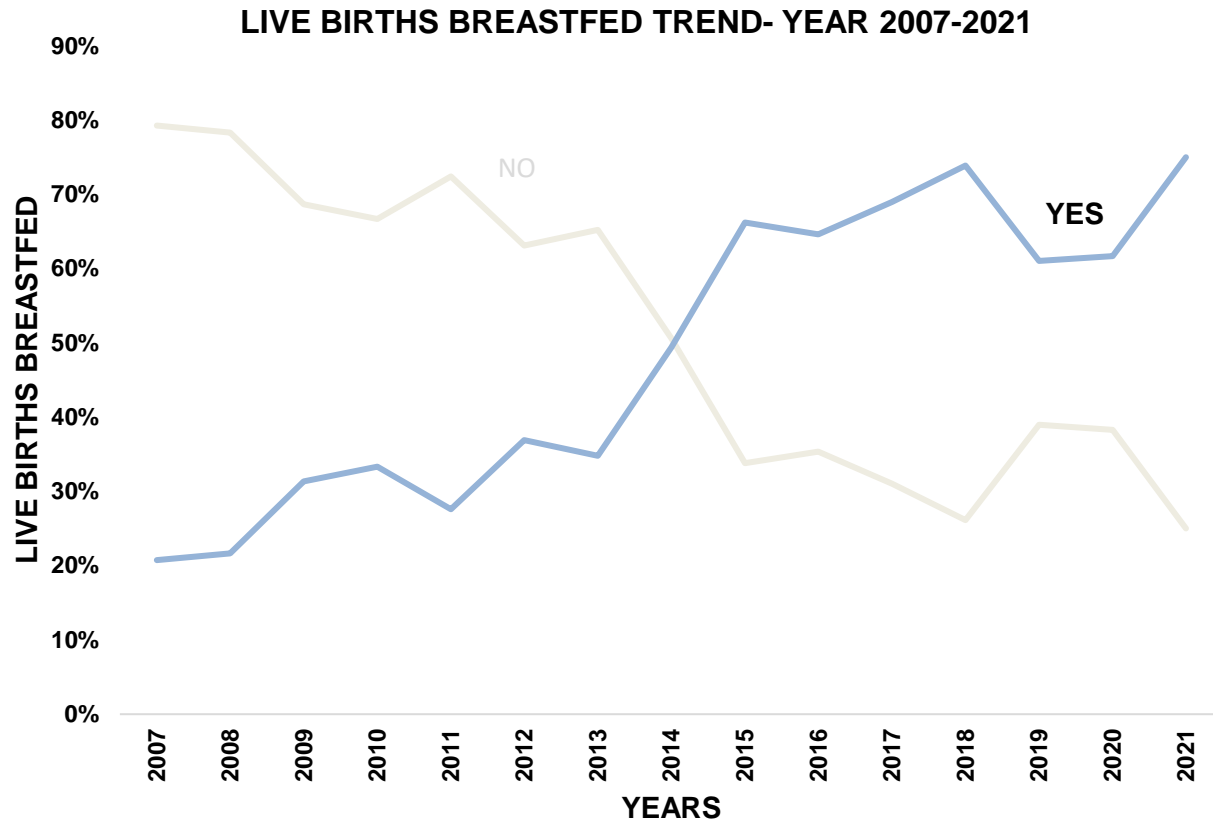
-  **Successful pregnancy is possible after lung transplantation**
-  **55% recipients transplanted for cystic fibrosis**
-  **High incidence of HTN and DM**
-  **High incidence of prematurity and low birth weight infants**
-  **High incidence of rejection during pregnancy (16%) and post-partum (14%)**
-  **Potential negative impact of rejection on graft and patient survival**
-  **Counseling regarding high rate of maternal complications and limited maternal survival**

Breastfeeding After Transplant



- ❖ **Recent studies have shown that transplant recipients taking prednisone, azathioprine, cyclosporine and tacrolimus need not be discouraged from breastfeeding.**
- ❖ **There are very limited data regarding breastfeeding while on mycophenolic acid products, sirolimus, everolimus and belatacept.**

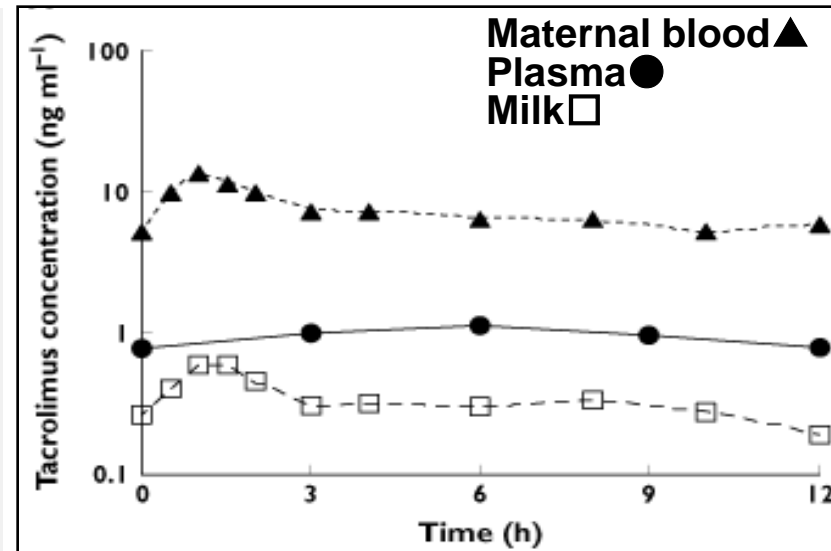
TPRI: Trend in Breastfeeding Practices



Breastfeeding

- ❖ Tacrolimus levels in blood and breast milk¹
 - ❖ Infant exposure through breast milk <0.3% of mother's weight-adjusted dose

- ❖ Tacrolimus levels in infants²
 - ❖ Among 15 infants, 11 exclusively breastfed
 - ❖ No difference in tacrolimus levels between breastfed and formula fed infants



Logarithmic scale

Fathered Pregnancies: MPA Exposed vs. Unexposed



	MPA Exposed	Unexposed to MPA	p-value (Chi ² or t-test)
Pregnancy outcomes	295	1092	
Miscarriages	9.2%	6.2%	NS
Stillbirths	0.7%	0.7%	NS
Ectopic pregnancies	0	0.6%	NS
Terminations	0	0.6%	NS
Live births	90.2%	91.9%	NS
Neonatal deaths	0.4%	0.6%	NS
Gestational age (wks)	39 ± 2.5	39 ± 2.3	NS
Preterm (<37 wks)	12.8%	12.8%	NS
Birth weight (g)	3323 ± 635	3362 ± 592	NS
LBW (<2500 g)	8.5%	6.6%	NS
Birth defects	3.5%	3.1%	NS

NS=not significant

- ❖ **Overall, the outcomes of pregnancies fathered by transplant recipients are like that of the general population.**
- ❖ **Currently, TPRI data does *not* support the avoidance of MPA for *male* transplant recipients considering parenthood.**

Pregnancy After Transplantation: Summary

- ❖ **Recipients of childbearing age should be counseled regarding feasibility and timing of pregnancy after transplantation.**
- ❖ **Pregnancy and maternal outcomes vary based on multiple factors, especially on the type of organ transplanted, pre-pregnancy transplant function, and other medical conditions.**
- ❖ **All pregnancies after transplantation are high risk due to increased percentages of high blood pressure, preeclampsia, and prematurity.**
- ❖ **All post-transplant pregnancies should be managed by multidisciplinary teams.**

WEBSITE: www.transplantpregnancyregistry.org

Questions?

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The screenshot shows the homepage of the Transplant Pregnancy Registry International. At the top left is the logo, which consists of a stylized heart and two figures, with the text "Transplant Pregnancy Registry International" and "A DIVISION OF GIFT OF LIFE INSTITUTE" below it. To the right of the logo are three green buttons: "CONTACT US", "SUPPORT OUR STUDY", and "CONNECT" with a Facebook icon. Below these is a blue navigation bar with white text links: "ABOUT US", "HOW TO PARTICIPATE", "PUBLICATIONS/COLLABORATIONS", "OUR TEAM", "STORIES", and "NEWS & EVENTS". The main content area features a large background image of hands being held together. Overlaid on this image is a blue rectangular box with white text that reads: "Studying post-transplant parenthood and effects of medications on fertility and pregnancy". At the bottom of the page, there are three smaller images in a row, each with a caption below it: 1. A group of people, including children and adults, gathered around a computer monitor. Caption: "JOIN THE REGISTRY". 2. Three women standing outdoors in front of a garden. Caption: "REGISTRY STORIES". 3. Four women standing together indoors. Caption: "MEET OUR TEAM".