

Outcomes of Pregnancies in Female Heart Transplant Recipients

Michael J. Moritz, MD

Chief Transplant Services, Lehigh Valley Health Network, Allentown, PA

Principal Investigator, TPR, Philadelphia, PA

Professor of Surgery, Morsani College of Medicine, Tampa, FL



Disclosure



Funding for the Transplant Pregnancy Registry International (TPR) is supported by grants from:

Astellas Pharma US, Inc.
Bristol-Myers Squibb.
Veloxis Pharmaceuticals

Background



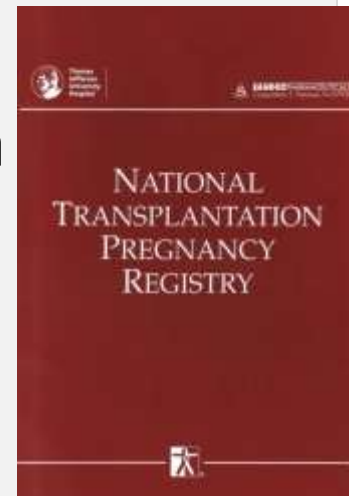
- ❖ **The first successful pregnancy post heart transplant occurred in 1988 in a female recipient who received her transplant for dilated cardiomyopathy.**
- ❖ **She conceived on cyclosporine and prednisone.**
- ❖ **She delivered a healthy infant at 31 weeks weighing 1450 g**
- ❖ **Both were reported healthy at 7 months postpartum**

Lowenstein BR, Vain NW, Perrone SV, et al. Successful pregnancy and vaginal delivery after heart transplantation. *Am J Obstet Gynecol* 1988;73:667-83.

Background



- ❖ **The Transplant Pregnancy Registry International (TPR) is a voluntary pregnancy registry which has been collecting pregnancy information for over 25 years.**
- ❖ **The TPR uses a simple, multipronged, IRB-approved 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



TPR: Pregnancy Outcomes in Female Transplant Recipients



Organ	Recipients	Pregnancies	Outcomes
Kidney	1,101	1,993	2,065
Liver	282	562	579
Liver-Kidney	11	16	17
Intestine	2	3	3
Kidney-pancreas	63	112	119
Pancreas alone	6	14	15
Heart	92	160	165
Heart-kidney	2	2	2
Heart-lung	6	6	6
Lung	33	44	46
Totals	1,599	2,912	3,017

Prepregnancy Recommendations



- ❖ **Good general health for at least 1 year since transplant**
- ❖ **No or minimal proteinuria**
- ❖ **No hypertension or well-controlled hypertension**
- ❖ **No rejection in the last year prior to pregnancy**
- ❖ **On maintenance immunosuppression compatible with pregnancy, i.e. NO mycophenolate**

Maintenance Immunosuppression



- ❖ **Generally considered “safe”**
 - cyclosporine, tacrolimus, prednisone, azathioprine
- ❖ **Contraindicated during pregnancy**
 - mycophenolate mofetil, mycophenolic acid
- ❖ **Not enough information to assure safety**
 - belatacept, sirolimus, everolimus

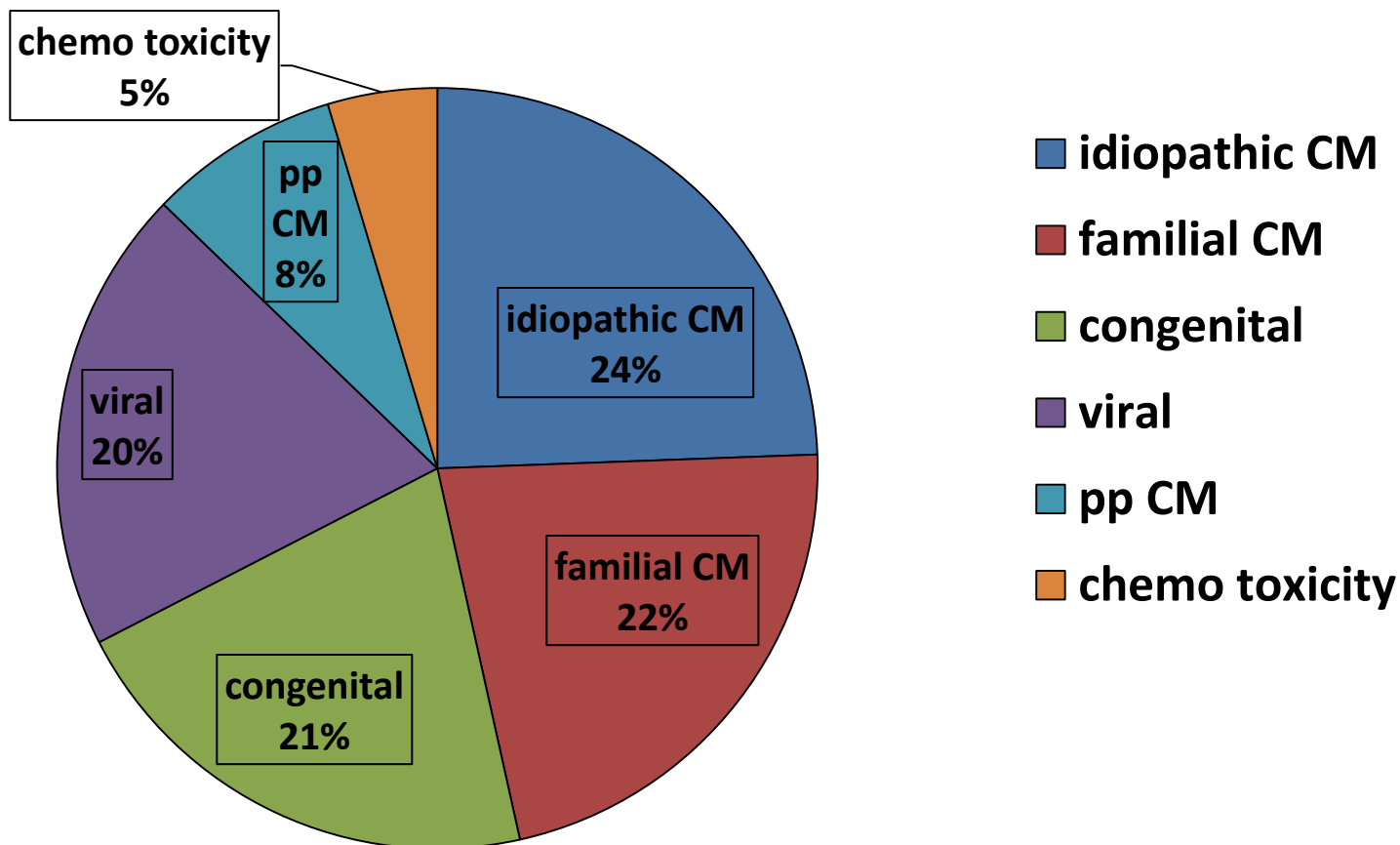
Heart Transplant Recipients: Maternal Factors



	86 recipients 147 pregnancies 152 outcomes*
Mean age at first transplant (yrs)	20 ± 8 Range 0.05-36.7
Mean transplant to conception interval (yrs)	6.9 ± 5.4 Range 0.1 -23.6
Unplanned	45%
Conception range	June 1987-July 2015

*includes multiple births

Heart Transplant Recipients: Indications for Heart Transplant



Heart Transplant Recipients: Pregnancy Outcomes



	86 recipients 147 pregnancies 152 outcomes
Live births	66% (101)
Miscarriages	27%
Terminations	5%
Stillbirths	1%
Ectopic	1%

Heart Transplant Recipients: Comorbid Conditions



	86 recipients 147 pregnancies 152 outcomes
Hypertension treated	45%
Preeclampsia	24%
Diabetes treated	7.6%
Rejection*	10%
Rejection episode postpartum (3 mos)*	7%
Graft loss within 2 years of pregnancy	2%

*any biopsy-proven rejection

Heart Transplant Recipients: Rejection During Pregnancy



Case	Rejection Grade	Treatment	Current Graft Status	Outcome
1 (2 biopsies)	1;3	None; increase prednisone	Died 5.6 yr PP	34 wks, 1814 g
2 (pregnancy #1)	2	Prednisone	Died 5.5 yr PP	8 wks termination
2 (pregnancy #2)	2;2	None		40 wks, 3813 g
3 (2 biopsies)	2;1A	None	Adequate	30 wks, 1191 g
4	Moderate	Methylprednisolone	Adequate	33 wks, 2240 g
5 (pregnancy #1)	1A	None	Died 12.2 yrs PP	12 wks miscarriage
5 (pregnancy #2)	2	None		30 wks, 1673 g
6	2	Methylprednisolone	Died 10.8 yr PP	34 wks, 2381 g

PP (postpartum); AMR (antibody mediated rejection); ATG (antithymocyte globulin); IVIg (intravenous immunoglobulin)

Heart Transplant Recipients: Rejection During Pregnancy



Case	Rejection Grade	Treatment	Current Graft Status	Outcome
7	Mild	Increase prednisone	Adequate	32 wks, 2523 g
8	3A	Oral steroid pulse	Died 16.4 yr PP	40 wks, 2495 g
9 (2 biopsies)	1B; 1A	Increase cyclosporine; none	Died 2.7 yr PP	stillbirth
10	Cellular and AMR	ATG, methylprednisolone, plasmapheresis and IVIg	Died during delivery	26 wks, 879 g
11	Mild	None	Adequate	39 wks, 2801 g
12	1B and AMR	Postpartum methylprednisolone, IVIg, plasmapheresis, rituximab	Adequate	early miscarriage

Heart Transplant Recipients: Newborn outcomes



	86 recipients 147 pregnancies 152 outcomes
Live births	101
Mean gestational age (wks)	36.2 ± 3.5
Premature (<37 wks)	43%
Mean birthweight (g)	2561 ± 697
Low birthweight (<2500 g)	40%
Cesarean section	45%

Heart Transplant Recipients: Child follow-up



	86 recipients 147 pregnancies 152 pregnancies
Live births	101
Birth defects	8/101 (7.9%)
Mean follow-up (yrs)	7.8 ± 6.2

Heart Transplant Recipients: Offspring birth defects



Birth defect	Immunosuppressive exposures during pregnancy	Treatment
Undescended testicle	Tacrolimus, azathioprine, prednisone	Corrective surgery
Pectus excavatum	Cyclosporine, azathioprine, prednisone	Corrective surgery
Duodenal atresia, AV canal defect, Tetralogy of Fallot	Tacrolimus, MPA	Multiple corrective surgeries
Cystic hygroma	Tacrolimus, everolimus	None
Facial deformities	Cyclosporine, sirolimus, MPA	Multiple corrective surgeries
Laryngomalacia	Tacrolimus, MPA, prednisone	Multiple surgical interventions
Hypospadias	Cyclosporine, prednisone	Corrective surgery
Vermian hypoplasia of cerebellum (Dandy-Walker variant)	Cyclosporine, sirolimus	None

Heart Transplant Recipients: Maternal follow-up





	86 recipients 147 pregnancies 152 outcomes
Mean follow-up (yrs)	8.2 ± 6.3
Adequate transplant function	63%
Maternal deaths	31%
Average age of child at maternal death (yrs)	9.6 ± 5.4 30 children

Important considerations in pregnancy after heart transplant







- ❖ **The mother:** Risks to long-term health, parenting ability, and survival.
- ❖ **The allograft:** Potential during pregnancy for changes in drug metabolism that may increase the risk of rejection. Potential for risks of transplant dysfunction and/or loss related to the pregnancy itself.
- ❖ **The fetus/neonate:** Potential teratogenic risks associated with medications. Potential for prematurity and low birth weight.
- ❖ **Family and social issues:** The ability of the family to cope with the mother's future unexpected illnesses and/or graft dysfunction while raising a child. The impact on the child if the mother is ill or dies.

Summary

-  Although pregnancy historically was discouraged for cardiac transplant recipients, the majority of reported pregnancies resulted in a live birth and negative effects on the transplanted heart due to pregnancy are uncommon.
-  Contraceptive counselling throughout the transplant process is necessary, as pregnancy may place some heart recipients, their transplant and their potential offspring at particular risk.

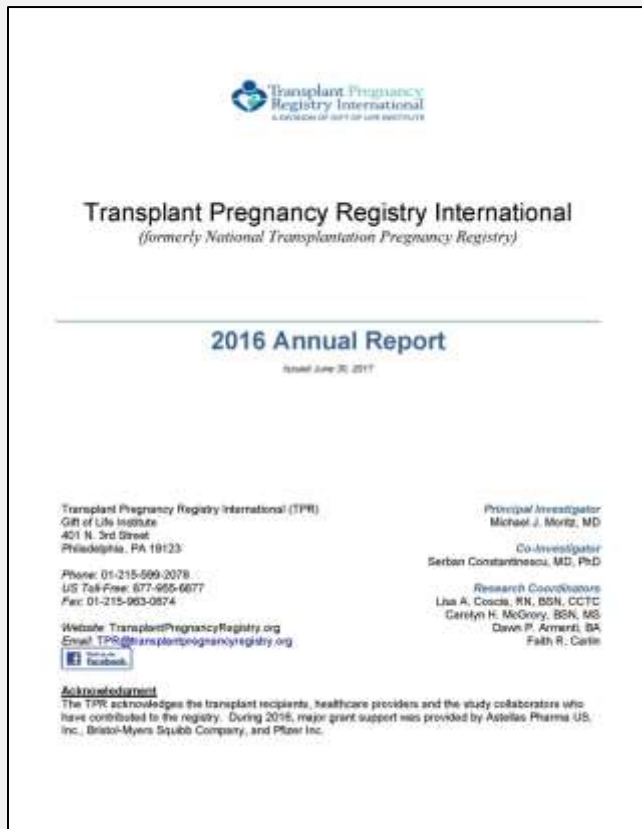
Summary

-  Ideally, post-transplant pregnancies should be planned with coordinated efforts between the recipient and her healthcare team.
-  Serious comorbidities commonly reported during pregnancies after heart transplantation include hypertension, preeclampsia and infection.
-  The cardiovascular changes that occur during pregnancy are typically well tolerated by the recipient.
-  Risks to the fetus include preterm delivery, low birth weight and in some cases, inheritable heart disease.

Summary



The TPR also serves as a resource for recipients who are making family planning decisions.



Annual Report available upon request.

Contact Information



How to reach the **TPR**
to report pregnancies or
request information:

Email: TPR@TransplantPregnancyRegistry.org

Toll-free (US): 877-955-6877
Outside US: 01-215-599-2078

Website: [TransplantPregnancyRegistry.org](https://www.transplantpregnancyregistry.org)

Recipient participation:
<https://www.tpr-international.org/>