Kidney Transplantation and Pregnancy

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- Female Transplant Recipients **Can and Do** Become Pregnant
- Pregnancy after kidney transplantation is not a “zero-risk” choice *(Cabiddu G, et al. J Nephrol 2018)*

Important Date-March 1958

- Edith Helm and her donor (identical twin sister)
- First woman in the world-successfully gave birth in 1958 after kidney transplantation (had 2 pregnancies)
- Her donor also had 4 healthy pregnancies

- The first post-kidney transplant pregnancy- reported by Dr. Joseph Murray and colleagues in 1963 (NEJM)
- Dr. Murray was awarded the Nobel Prize for Medicine in 1990

Questions

- Is pregnancy advisable in transplant recipients?
- Will pregnancy be complicated?
- Will the baby be healthy?
- Will there be any long-term harm (mother and the baby)?

Case

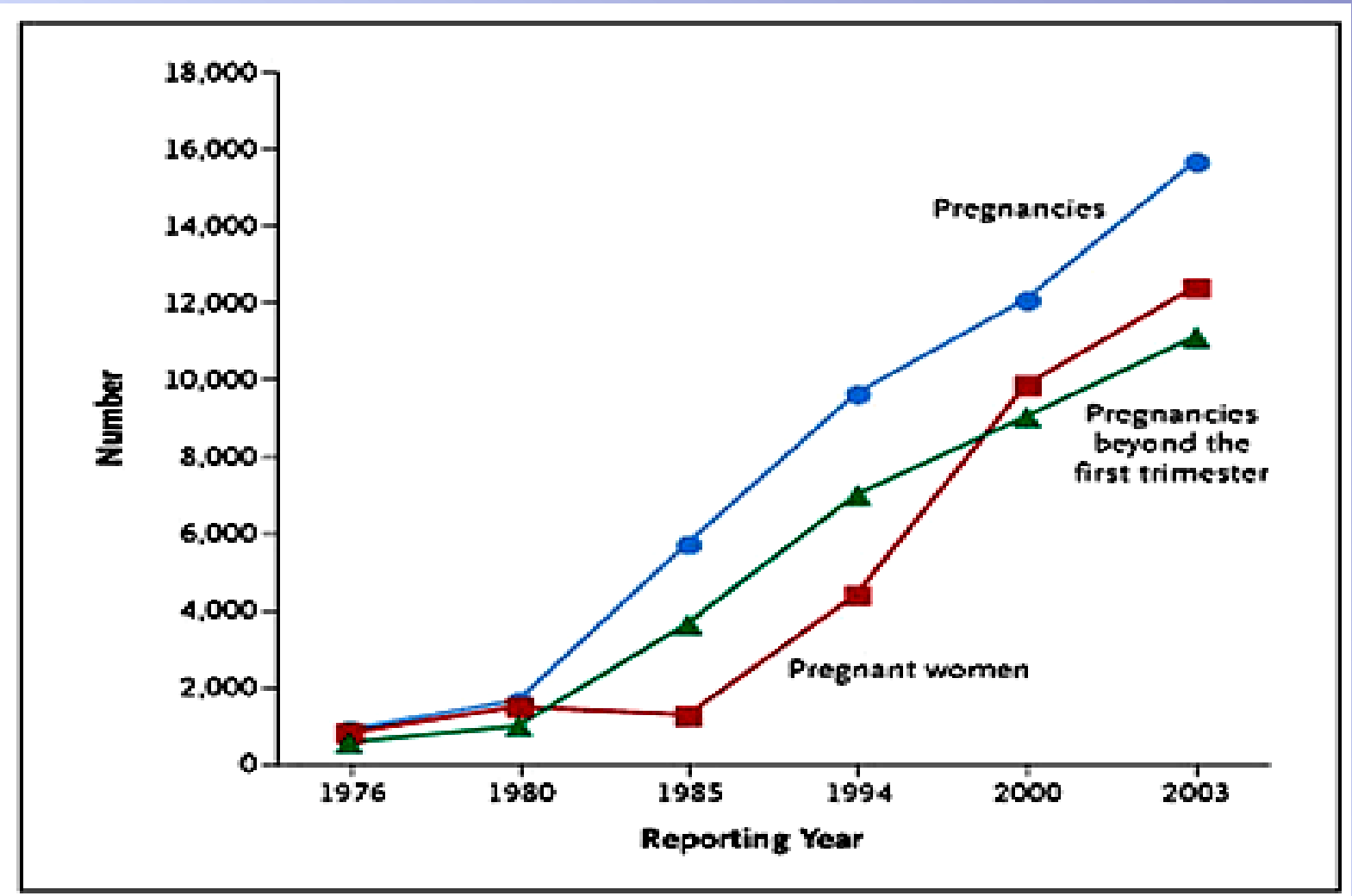
- 35 year old **AA female**
- ESRD: due to FSGS and HTN; has sickle cell trait
- Living-related kidney transplant
- On tacrolimus 6 mg bid, **MMF 500 mg bid** and prednisone 5 mg qd; also on lisinopril
- BP 120/80 mmHg, Scr 1.3 mg/dl, urine protein/creat ratio: 0.05
- She wants to have a baby (clinic visit **17 months posttransplant**)

Kidney Transplantation and Pregnancy

- Registries:
  - US National Transplantation Pregnancy Registry-established in 1991-as of December 2017, total 2,912 pregnancies in 1,599 female recipients and 1,396 pregnancies fathered by 896 recipients
  - UK Transplant Pregnancy Registry-established in 1997
  - Australia/New Zealand Registry
  - EDTA European Registry
- Case reports and retrospective single center studies

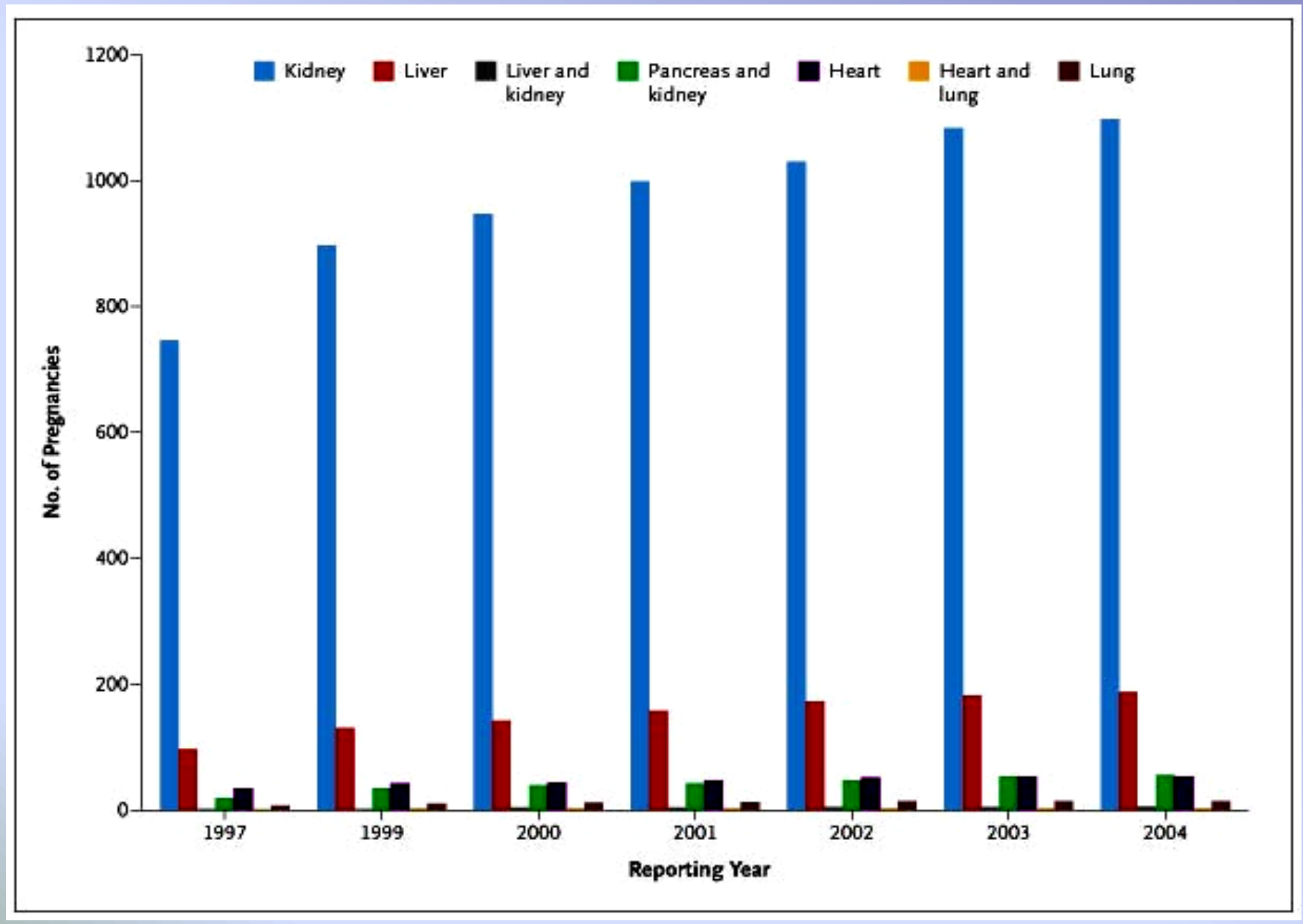
Kidney Disease-Facts

- Majority of women with CKD/ESRD are beyond childbearing age; libido decreased/not sexually active
- As renal function declines, fertility rates decline proportionately, largely due to dysregulation in the hypothalamic–pituitary–ovarian axis
- The frequency of conception is decreased in women with CKD and markedly decreased in ESRD
- **Return of fertility in 1-12 months is the rule in transplant recipients** (not known if the recovery is complete)
  - Study in 309 transplant recipients, 44% were not aware that a woman could become pregnant after transplantation; most pregnancies were planned
    French VA, et al. Obstet Gynecol 2013



•Pregnancies in Kidney Transplant Recipients Reported Worldwide-3 Registries

McKay D and Josephson M, NEJM 2006

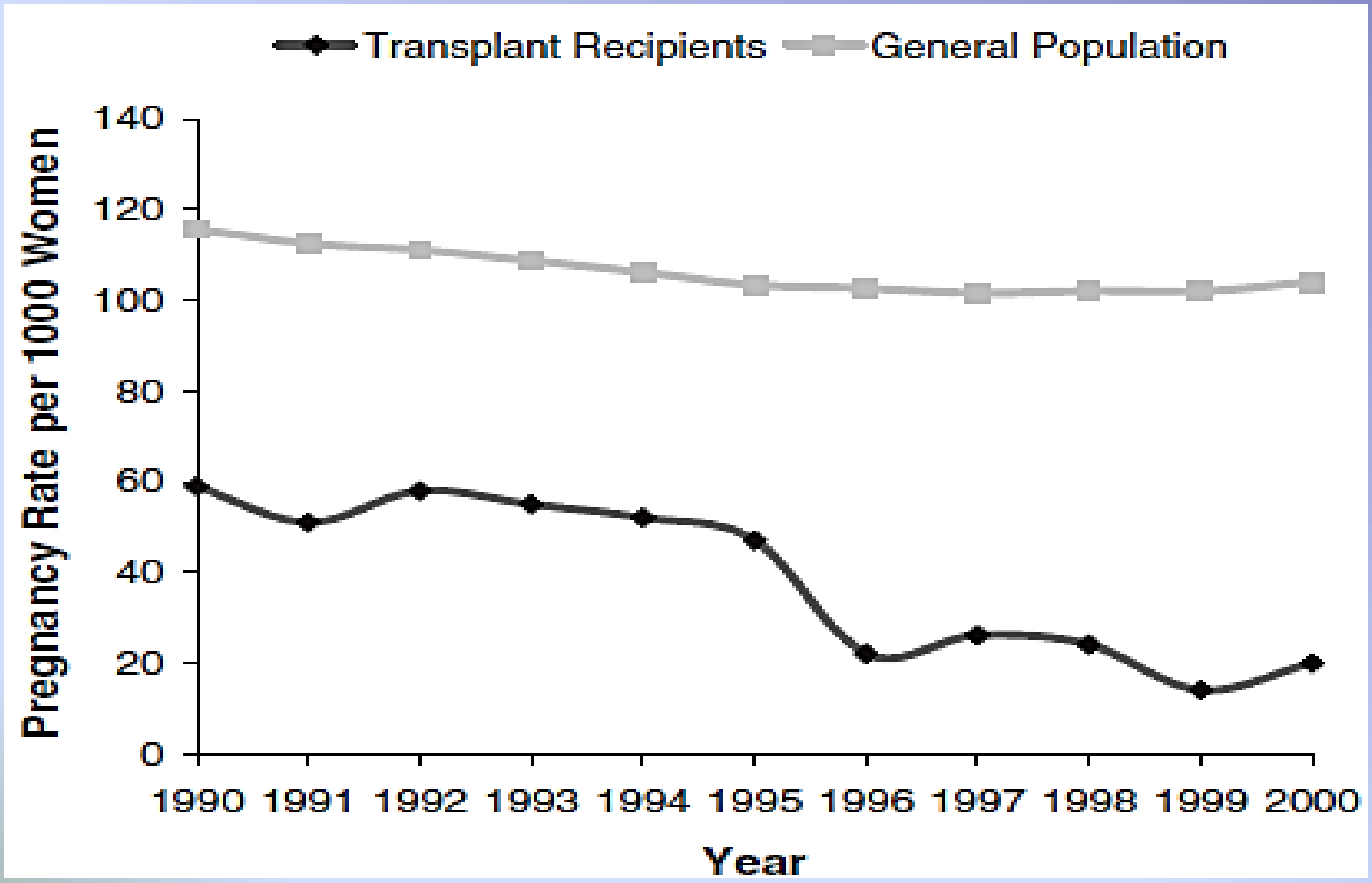


McKay D and Josephson M, NEJM 2006

Fertility-Kidney Transplantation

- Observational study of 16,195 female kidney transplant recipients aged 15–45 years in the United States between **1990 and 2003**
- The pregnancy rate and live birth rate using Medicare claims data from the **first 3 posttransplant** years

Gill JS, et al. Am J Transplant 2009



•Pregnancy rate in transplant recipients-markedly lower among women transplanted in more recent years-*1995

Table 4: Fetal outcomes by posttransplant year of conception[1]

Fetal outcome	Any year (N = 453) N (%)	Year 1 (N = 152) N (%)	Year 2 (N = 184) N (%)	Year 3 (N = 117) N (%)
Live births	251 (55.4)	68 (44.7)	110 (59.8)	73 (62.4)
Fetal loss	202 (44.6)	84 (55.3)	74 (40.2)	44 (37.6)
Therapeutic abortion	17 (3.8)	7 (4.6)	6 (3.3)	4 (3.4)
Other fetal loss	185 (40.8)	77 (50.7)	68 (37.0)	40 (34.2)
Spontaneous abortion	96 (21.2)	36 (23.7)	38 (20.7)	22 (18.8)
Abortion not otherwise specified	65 (14.3)	32 (21.1)	22 (12.0)	11 (9.4)
Stillbirth	7 (1.5)	2 (1.3)	4 (2.2)	1 (0.9)
Ectopic pregnancy	12 (2.6)	3 (2.0)	4 (2.2)	5 (4.3)
Abnormal product of conception	5 (1.1)	4 (2.6)	0	1 (0.9)

[1]Fetal outcomes could be determined in 453 of 530 pregnancies.

- Only **55.4% of pregnancies** ended in **a live birth**, a proportion far lower than the 74–79% previously reported in studies from voluntary registries-registries may have underestimated fetal loss
- The pregnancy rate after kidney transplantation was far lower and declined more rapidly than reported in the general American population

Gill JS, et al. Am J Transplant 2009

Fertility-Kidney Transplantation

- Limitations:
  - Only included Medicare-insured patients and provides information regarding pregnancy only during the first three posttransplant years while patients maintained Medicare insurance coverage
  - No information regarding immunosuppressant drug use at the time of pregnancy
  - No information regarding the incidence of birth defects

Gill JS, et al. Am J Transplant 2009

Pregnancy Outcomes

Pregnancy Outcomes

- Meta-analysis of articles published between 2000 and 2010 that reported pregnancy-related outcomes among kidney transplant recipients
- 50 studies: 4706 pregnancies in 3570 kidney transplant recipients
- 18 studies were from Europe, 12 from the Middle East, 8 from Asia, 6 from North America, 4 from South America and 2 from Australia

Deshpande NA, et al. Am J Transplant 2011

Table 2. Maternal [1] demographics, pregnancy outcomes, obstetric complications and delivery outcomes among kidney transplant recipients

Maternal demographics	Mean	USA, 2006 [2]
Age at pregnancy	29.0 years (28.9–29.1)	NA
Transplant-pregnancy interval	3.2 years (3.1–3.3)	NA
Pregnancy outcome	Pooled incidence	USA, 2006
Live birth	73.5% (72.1–74.9)	66.7% [3]
Miscarriage [4]	14.0% (12.9–15.1)	17.1% [3]
Abortion [5]	9.5% (8.6–10.4)	NA
Stillbirth	2.5% (2.0–3.0)	NA
Ectopic pregnancy	0.6% (0.4–0.9)	NA
Obstetric complication	Pooled incidence	USA, 2006
Hypertension [6]	54.2% (52.0–56.4)	NA
Preeclampsia	27.0% (25.2–28.9)	3.8%
Gestational diabetes	8.0% (6.7–9.4)	3.9%
Delivery outcome	Mean/Pooled incidence	USA, 2006
Cesarean section	56.9% (54.9–58.9)	31.9%
Preterm delivery [7]	45.6% (43.7–47.5)	12.5%
Gestational age	35.6 weeks (35.5–35.7)	38.7 weeks
Birth weight	2420 grams (2395–2445)	3298 grams

- Complications of **preeclampsia (27.0%), gestational diabetes (8.0%), C-section (56.9%)** and **preterm delivery (45.6%)** were higher than the general US population (3.8%, 3.9%, 31.9% and 12.5%, respectively)

Deshpande NA, et al. Am J Transplant 2011

Pregnancy Outcomes

- Women who had a kidney transplant in childhood (aged <18 years; child-tx mothers-101 pregnancies in 66 pts) compared to women who had a transplant in adulthood (aged ≥18 years; adult-tx mothers-626 pregnancies in 401 pts)
- Observational cohort study in the Australia and New Zealand Dialysis and Transplant Registry-at least 1 pregnancy was reported between January 1963, and December 2012

Wyld M, et al. JAMA Pediatr 2015

Outcome	Child-Tx Mothers[a]		Adult-Tx Mothers[a]		*P* Value
	No.	Value	No.	Value	
Pregnancy outcome, No. (%)	101		626		
Live birth		77 (76)		485 (77)	
Stillbirth		5 (5)		14 (2)	
Abortion		4 (4)		61 (10)	
Termination		14 (14)		65 (10)	
Other		1 (<1)		1 (<1)	
Birth weight, mean (SD), g	23	2365 (777)	173	2545 (741)	.28
Gestational age, mean (SD), wk	29	35 (5)	198	36 (4)	.68

- During the 5 decades data have been collected; the termination rate decreased from 33% of all pregnancies (between 1963-1972) to 3% of all pregnancies (between 2003 and 2012)
- Live birth rates: similar for child-tx and adult-tx mothers
- Preeclampsia-in 28% of pregnancies for both groups, 4 to 5 times higher than in the general population
- Pregnancy outcomes for child-tx mothers are similar to those for adult-tx mothers

Pregnancy Outcomes-Meta-analysis

- 87 studies; 6712 pregnancies in 4174 kidney transplant recipients
- The live-birth rate was 72.9%
- Induced abortions (12.4%; 95% CI, 10.4–14.7)
- Miscarriages (15.4%; 95% CI, 13.8–17.2)
- Stillbirths (5.1%; 95% CI, 4.0–6.5)
- Ectopic pregnancies (2.4%; 95% CI, 1.5–3.7)

Shah, S, et al. BMC Nephrology 2019

Pregnancy Outcomes-Meta-analysis

- Preeclampsia (21.5%; 95% CI, 18.5–24.9)
- Gestational diabetes (5.7%; 95% CI, 3.7-8.9)
- Pregnancy induced hypertension (24.1%; 95% CI, 18.1–31.5)
- Cesarean section (62.6, 95% CI 57.6–67.3)
- Preterm delivery was 43.1% (95% CI, 38.7–47.6)
- The rate of spontaneous abortion was higher in women with mean maternal age < 25 years and > 35 years as compared to women aged 25–34 years

Shah, S, et al. BMC Nephrology 2019

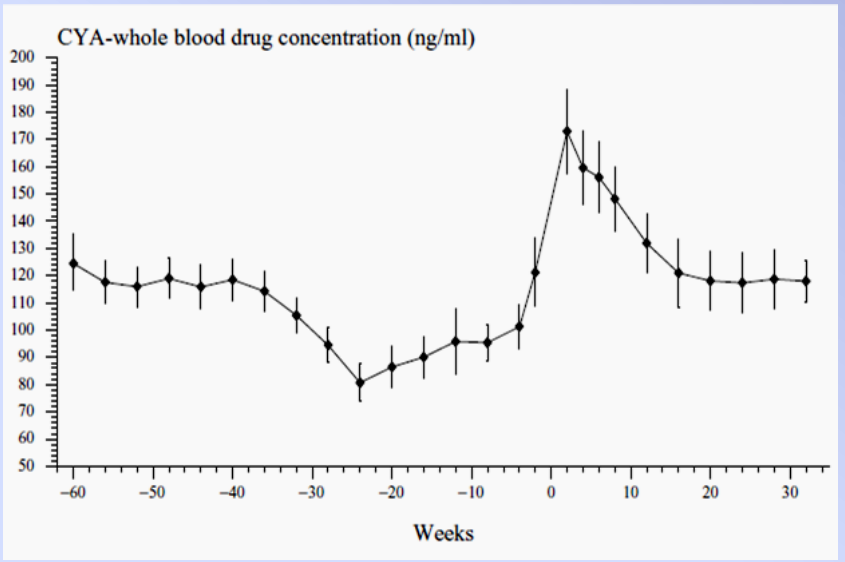
Outcomes

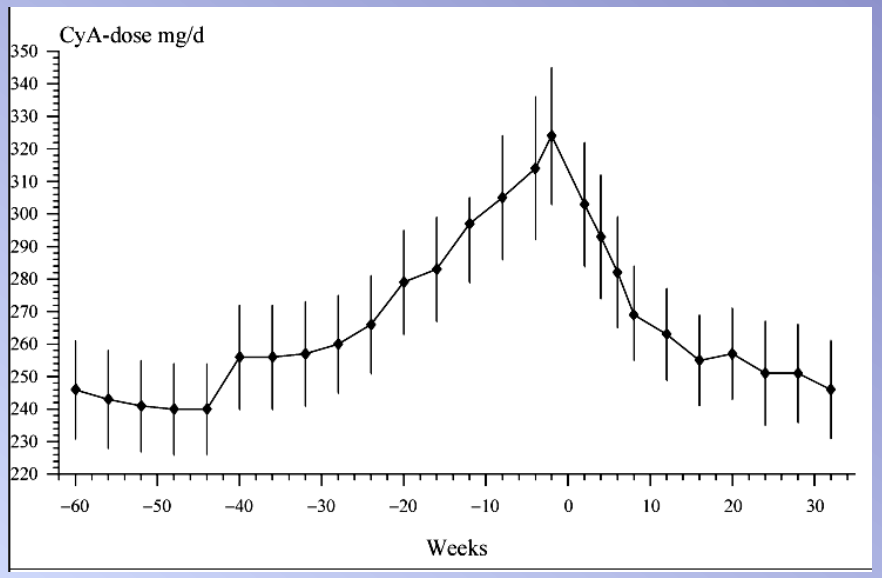
- Maternofetal outcomes from Italy-less favorable in CKD and KTx as compared with the low-risk population; CKD stage and HTN are important determinants of results *Piccoli GB, et al. Transplantation 2017*
- From Italy-data 2000-2012; women on dialysis have a 10-fold lower probability of delivering a live-born baby than those who have undergone **KTx**, who in turn have a **10-fold lower probability** of delivering a live-born baby as compared with the overall population *Piccoli GB, et al. Nephrol Dial Transplant 2014*
- Potential predictive factors for poor pregnancy outcome: 1 previous kidney transplant (P=0.03), first trimester serum creatinine >125 mmol/L (P=0.001), and diastolic BP >90 mmHg in the second (P=0.002) and third trimesters (P=0.05) *Bramham K, et al. CJASN 2013*

Pregnancy Outcomes

- 61 pregnancies-occurred in 46 patients-excluded 10 miscarriages during the first trimester
- The use of **tacrolimus** was an independent predictive factor for gestational diabetes
- De novo donor-specific anti-HLA antibodies were detected after only 5.9% of pregnancies (3/51): for two women, the father had the same HLA antigens as those from the deceased organ donor-the risk of **anti-HLA alloimmunization was low**

Hebral AL, et al. Nephrol Dial Transplant 2014





-A case-control study, five German transplant centers; 81 patients with pregnancies and 81 controls without pregnancies; 41 patients on AZA (25-175 mg/d)/steroids, 40 patients on cyclosporine

-10-year graft survival: 62.5% vs 67%; **No acute rejection**

-No differences between AZA and CsA groups

-CsA trough levels decreased significantly during pregnancy and increased after delivery

Fischer T, et al. Am J Transplant, 2005

Tacrolimus-Pregnancy

- In pregnant SLE patients, trough concentrations of TAC significantly decreased in the second trimester
- It has been reported that the level of unbound TAC required for treatment does not decrease
- The concentrations of TAC in the umbilical cord blood were lower than those in the maternal blood
- The level of TAC in infant bloods was below detectable limits

Hiramatsu Y, et al. Lupus 2018

Tacrolimus-Pregnancy

- TAC highly bound to plasma proteins and erythrocytes: significant anemia and hypoalbuminemia could affect the levels
- Trough TAC-measured in whole blood; dosage titration to maintain trough concentrations might lead to an increase in unbound (free fraction) TAC concentrations
- Metabolism: increased due to increased maternal CYP3A4 activity
  - 20-30% dose increase might be required to maintain levels
- Monitoring plasma or unbound tacrolimus trough concentrations (more costly and not routine), might better predict drug efficacy and toxicity

- Cyclosporine and tacrolimus levels MUST be checked frequently during pregnancy-must have adequate levels to prevent rejection

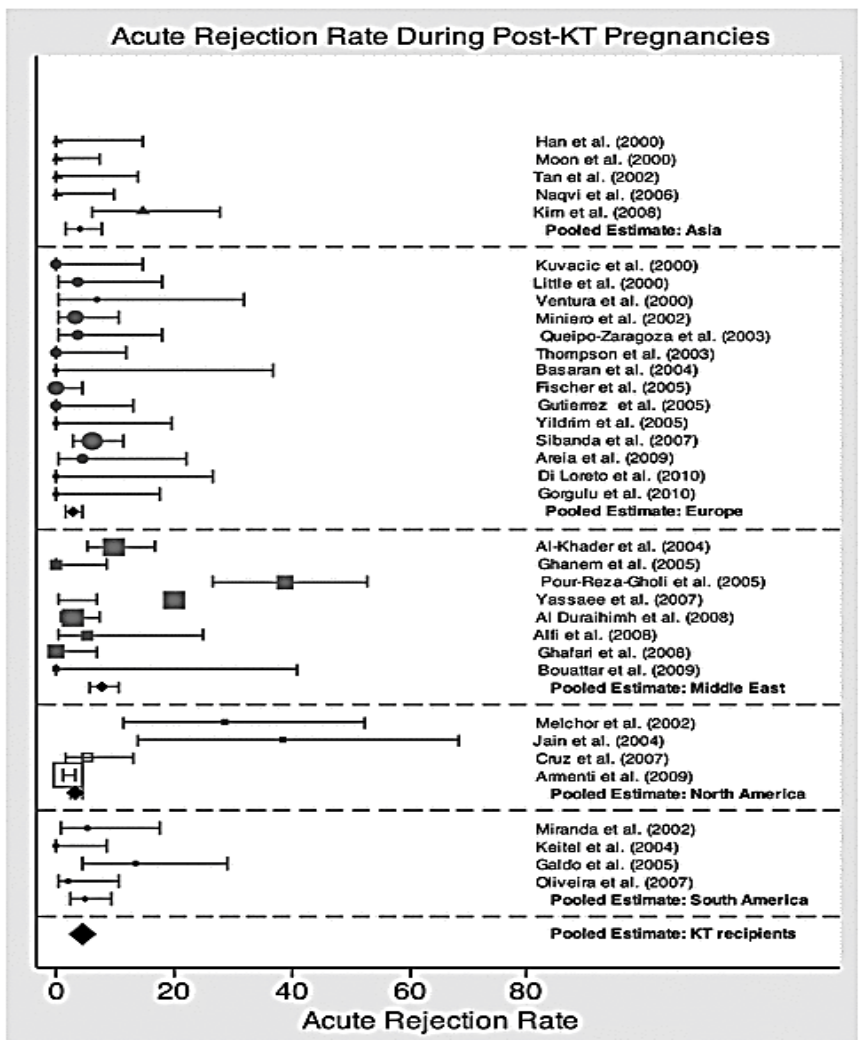
Pregnancy Outcomes

- 29 pregnancies in 23 patients-from Spain
- DD kidney transplants
- 26 live birth, one miscarriage, two stillbirths
- **Anemia very common (75%)**
- **AKI in 10.7% of pregnancies**
- Patient on MMF during pregnancy: newborn with cleft palate, external auditory canal atresia and micrognathia

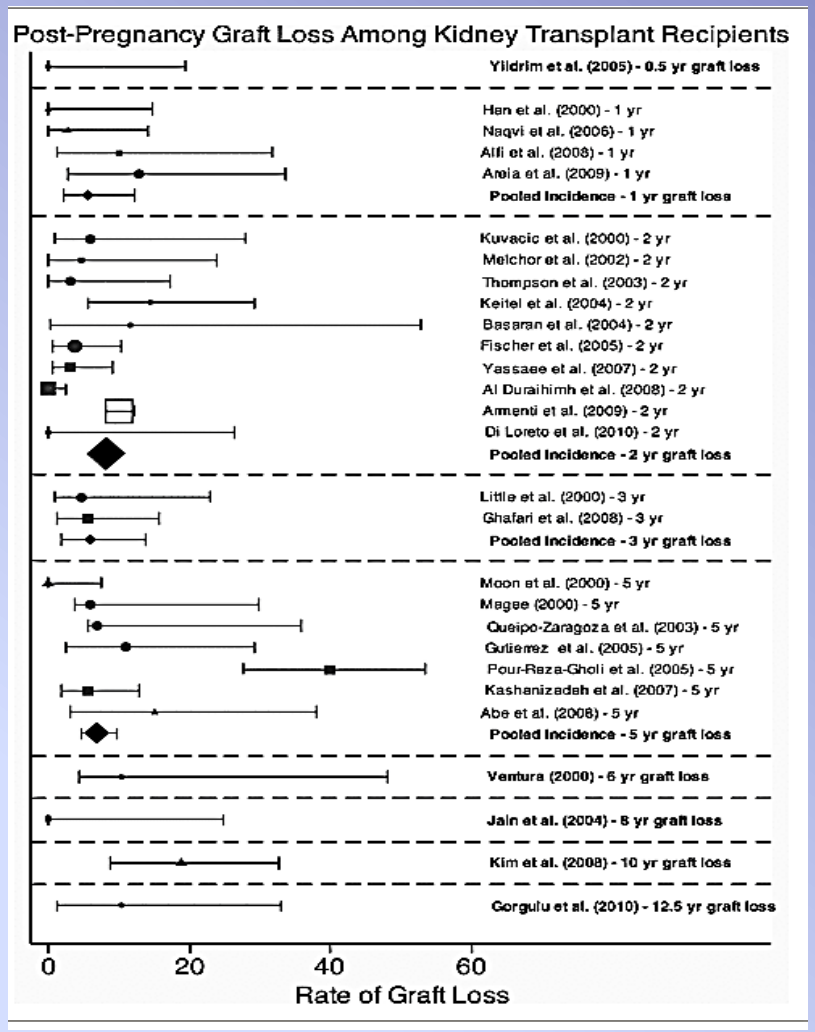
Perales-Puchalt A, et al. J Matern Fetal Neonatal Med 2012

Maternal Conditions/Risks

- Hypertension: worsens (25-73%)
- Preeclampsia: up to 28%
- Risk of ectopic pregnancy: not increased
- Worsening renal function
  - Acute rejection
  - Obstruction
- Increased likelihood of operative delivery: 30-59% C-section
- Graft loss after delivery: 4-13% within 2 years after delivery
- Diabetes: slightly higher



Acute rejection rate during post-KT pregnancies: Asia (4%), Europe (3%), Middle East (8%), North America (3%) and South America (5%). Overall pooled incidence of 4.2%.

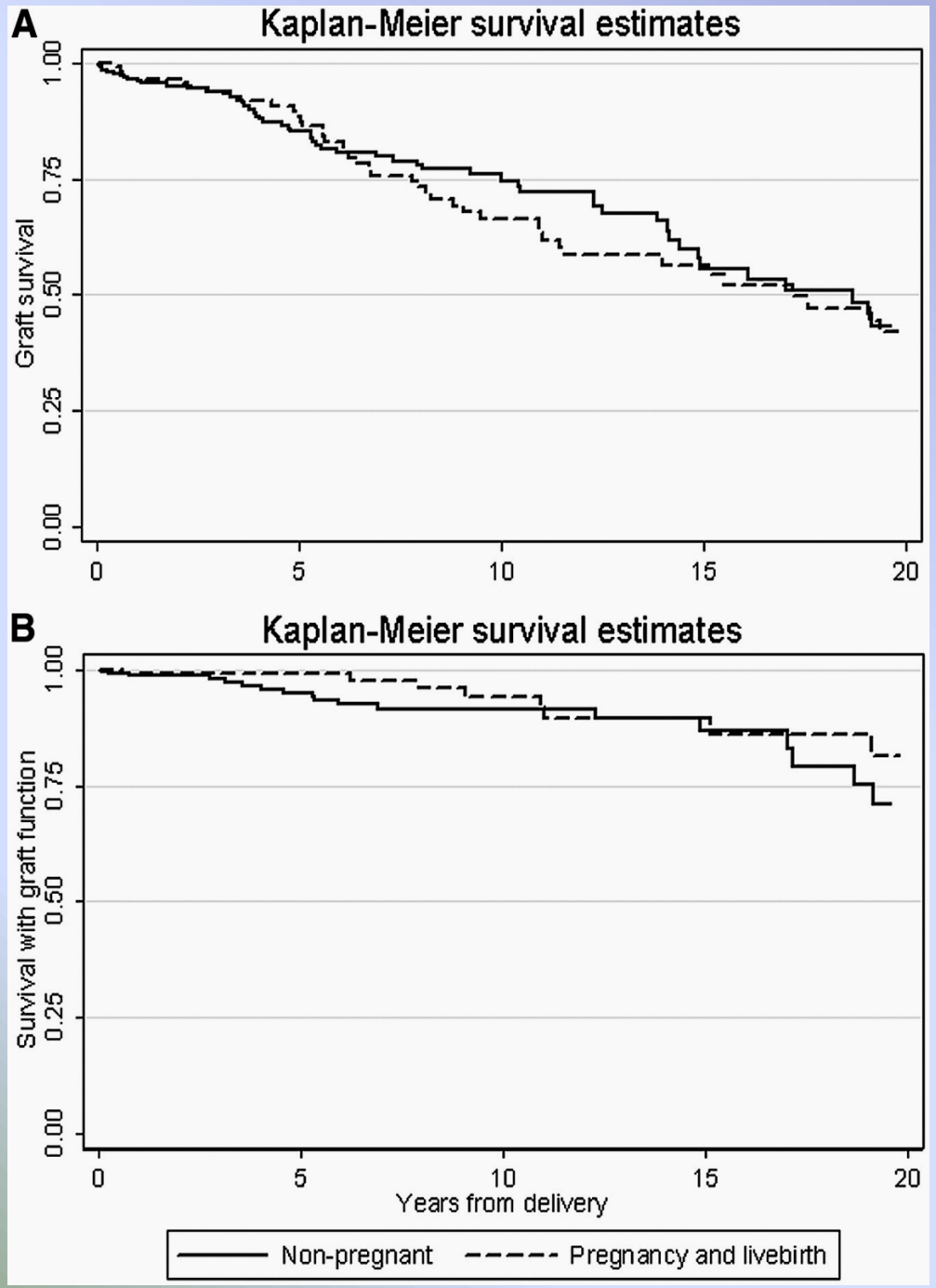


Postpregnancy graft loss, stratified by years of follow-up: 0.5 years (0%), 1 year (6%), 2 years (8%), 3 years (6%), 5 years (7%), 6 years (10%), 8 years (0%), 10 years (19%) and 12.5 years (11%).

Deshpande NA, et al. Am J Transplant 2011

Maternal Risks
Kidney Transplantation

- Acute rejection episode during pregnancy: 2-14% (vs 31% in lung transplants), treated with high-dose steroids
- Incidence of AR not increased dramatically-especially with adequate drug levels
- If chronic allograft dysfunction is present prior to pregnancy, greater risk of pregnancy-related graft loss



- Australian/New Zealand Dialysis and Transplant Registry-40 years of pregnancy-related outcomes for transplant recipients
- The mean age at the time of pregnancy during the last decade increased significantly to 32 years
- **Matched 120 parous with 120 nulliparous women**
- 577 pregnancies-a first live birth was **not associated with a poorer 20-yr graft or patient survival**
- 97% of this cohort became pregnant beyond their first transplantation year; **safe interval between tx and pregnancy seems to be 1 to 4 years**

Levidiotis V, et al. JASN 2009

Maternal Outcomes

- Retrospective cohort study of all Norwegian women receiving a kidney transplant before the age of 50, between 1969 and 2013, 650 women studies-124 had a pregnancy
- Transplant recipients with pregnancies had a low risk of subsequent graft loss or death (compared to transplant recipients without pregnancy)

Majak GB, et al. Transplantation 2018

Comorbid Factors-Pregnancy Outcome

- Etiology of original kidney disease (recurrence?-lupus or FSGS)
- Chronic allograft dysfunction
- Cardiovascular and pulmonary status
- Diabetes or hypertension
- Inherited diseases in mother or father
- Infections might affect the fetus: CMV, herpes simplex, toxoplasmosis, HBV, HCV (transmission?), BK virus
- Obesity

Immunosuppressive Medications and the Fetus

Potential Risks to Children Born to Transplant Recipients

- Preterm birth (14-83% vs 5-15% in general population)
- Intrauterine growth retardation (IUGR) and low birth weight (19-67% vs 5-13% in general population), neurocognitive and developmental disabilities
- Congenital abnormalities (no increase with CsA, chromosome aberrations with AZA)
- Adrenocortical insufficiency
- Hyperkalemia, renal dysfunction
- Immunologic abnormalities, malignancies
- Infections (CMV, hepatitis B and C-especially in liver transplant recipients, sepsis)

Fetal Safety for Commonly Used Immunosuppressive Drugs

	Pregnancy Category
• Corticosteroids	B
• Cyclosporine	C
• Tacrolimus	C
• Azathioprine	D
• Rapamycin	C
• **MMF**	**D**

A-no risk, B-low risk, C-risk can not be ruled out, D-known risk, X-contraindicated

Fetal Safety for Commonly Used Immunosuppressive Drugs

	Pregnancy Category
• Daclizumab (Zenapax)	C
• Basiliximab (Simulect)	B
• OKT3	C
• Thymoglobulin	C
• ATGAM	C

A-no risk, B-low risk, C-risk can not be ruled out, D-known risk, X-contraindicated

Pregnancy Outcome

	Renal transplantation	Primary renal disease	*P* value
Pregnancies	73	59	—
Spontaneous abortions	17 (23%)	9 (15%)	NS
Therapeutic abortions	7 (9.6%)	2 (3.4%)	NS
Births	49	48	—
Neonates	50	48	—
Superimposed preeclampsia	9 (19%)	10 (21%)	NS
Preterm delivery	29 (60%)	10 (21%)	0.001
IUGR	25 (52%)	8 (17%)	0.001
Cesarean delivery	18 (37%)	13 (27%)	NS
Hospitalization in NICU	17 (35%)	3 (6%)	0.01
Stillbirths	1 (2%)[a]	0	NS

	Renal transplantation (n = 48)[a]	Primary renal disease (n = 48)[a]	*P* value
Major malformations	2 (4.2%)	2 (4.2%)	NS
Mild errors of morphogenesis	10 (20.8%)	8 (16.6%)	NS

[a]Number of live births.

Bar J, et al. Am J Med Genet 2003

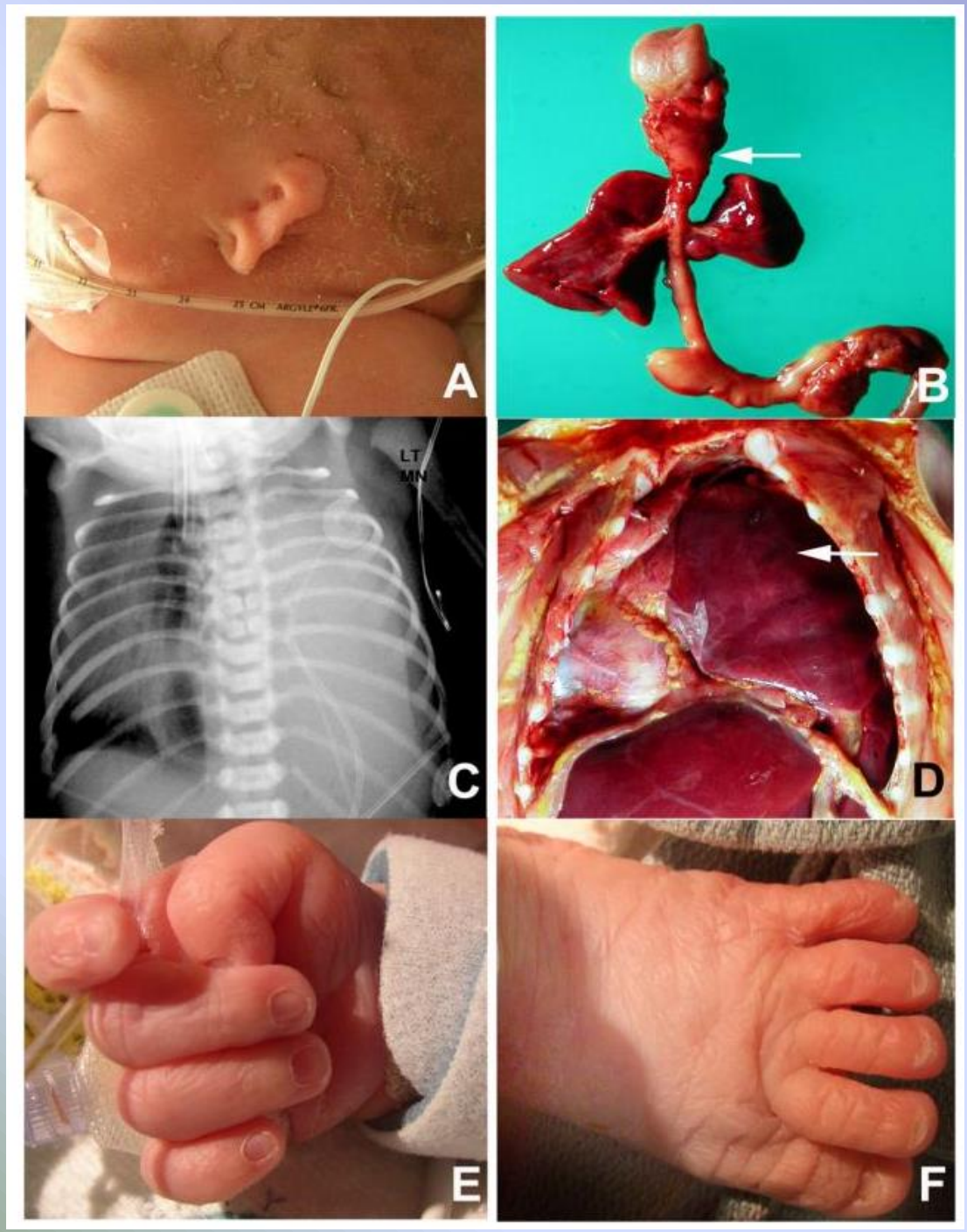
Immunosuppressive Drugs

- **Steroids:** decreased birth weight and head circumference, hyperactive behavioral problems-**OK to use**
- **CsA:** autoantibodies to gastric antigens, no increase in the incidence or pattern of specific malformations noted among the newborn with the use of CsA or azathioprine-**OK to use**

  Classen JB, et al. Transplantation 1991
- **CsA:** No teratogenic effect has been reported: 9.7% fetal loss and 3% malformations in 629 pregnancies- small fetal kidneys

Immunosuppressive Drugs

- **Tacrolimus:** toxicities dose-dependent, transient neonatal hyperkalemia, cardiomyopathy in twins-**OK to use**
- **MMF**: MMF embryopathy-hypoplastic toe nails, short fingers, cleft lip and palate, ear deformities, ocular anomalies, deformities of heart, kidneys and CNS, no chromosomal abnormalities-**NOT recommended**
- **Rapamycin** : teratogenic in rats, no structural abnormalities-**NOT recommended**



- A-Aural atresia, absent auditory canal, short neck
- B-Bilateral pulmonary hypoplasia, esophageal atresia
- C-bifid T6 and T7 vertebral bodies
- D-left chest occupied with abdominal organs
- E-right hand with short thumb and 5th digit
- F-left foot with hypoplastic toenails

Parisi MA et al. Am J Med Genet A, 2009

MYCOPHENOLATE REMS

MYCOPHENOLATE-RELATED RISK OF MISCARRIAGE AND BIRTH DEFECTS

Acceptable Contraception Methods			
Option 1 **Methods to Use Alone**	■ Intrauterine devices (IUDs) ■ Tubal sterilization ■ Patient's partner had a vasectomy		
OR			
Option 2 **Choose One Hormone Method AND One Barrier Method**	**Hormone Methods** choose 1		**Barrier Methods** choose 1
	Estrogen and Progesterone ■ Oral contraceptive pill ■ Transdermal patch ■ Vaginal ring **Progesterone-only** ■ Injection ■ Implant	AND	■ Diaphragm with spermicide ■ Cervical cap with spermicide ■ Contraceptive sponge ■ Male condom ■ Female condom
OR			
Option 3 **Choose One Barrier Method from each column (*must choose two methods*)**	**Barrier Methods** choose 1		**Barrier Methods** choose 1
	■ Diaphragm with spermicide ■ Cervical cap with spermicide ■ Contraceptive sponge	AND	■ Male condom ■ Female condom

Treatment of Hypertension

- Treatment of severe HTN (systolic BP ≥160 mmHg and/or diastolic BP ≥110 mmHg) persisting for ≥15 minutes-always recommended (to reduce the risk of maternal stroke and other serious maternal complications)
- For women with chronic nonsevere HTN with comorbid conditions, drug therapy should be used to keep systolic BP <140 mmHg and diastolic BP <90 mmHg
- ACE inhibitors (D) are **contraindicated** in pregnancy; less experience with ARBs-**not recommended**

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ORIGINAL ARTICLE

◄ Previous Volume 354:2443-2451 June 8, 2006 Number 23 Next ►

Major Congenital Malformations after First-Trimester Exposure to ACE Inhibitors

William O. Cooper, M.D., M.P.H., Sonia Hernandez-Diaz, M.D., Dr.P.H., Patrick G. Arbogast, Ph.D., Judith A. Dudley, B.S., Shannon Dyer, B.S., Patricia S. Gideon, R.N., Kathi Hall, B.S., and Wayne A. Ray, Ph.D.

-ACEi restricted to the first trimester of pregnancy, an exposure that was previously considered to be safe, was associated with a risk of a major congenital malformation that was **2.7 times as great as the risk** with no fetal exposure to ACE inhibitors or other antihypertensive medications

-Prespecified subgroup analyses identified significantly increased **risks of malformations of the cardiovascular and central nervous systems.** In a post hoc analysis, significantly **increased risk of kidney malformations was found.**

BP Medications

- **Methyldopa (C):** safe
- **Labetalol (C):** safe, less bradycardia than beta blockers
- **Calcium channel blockers (C):** safe in general, profound hypotension when used with magnesium, reserve for severe hypertension
- **Hydralazine (C):** safe, no increase in birth defects
- **Beta blockers(C):** probably safe, fetal bradycardia, respiratory depression at birth
- **Minoxidil (C):** limited experience, hypertrichosis in the infant

Breast-Feeding

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

Constantinescu S et al. Best Practice & Research Clinical Obstetrics & Gynecology 2014

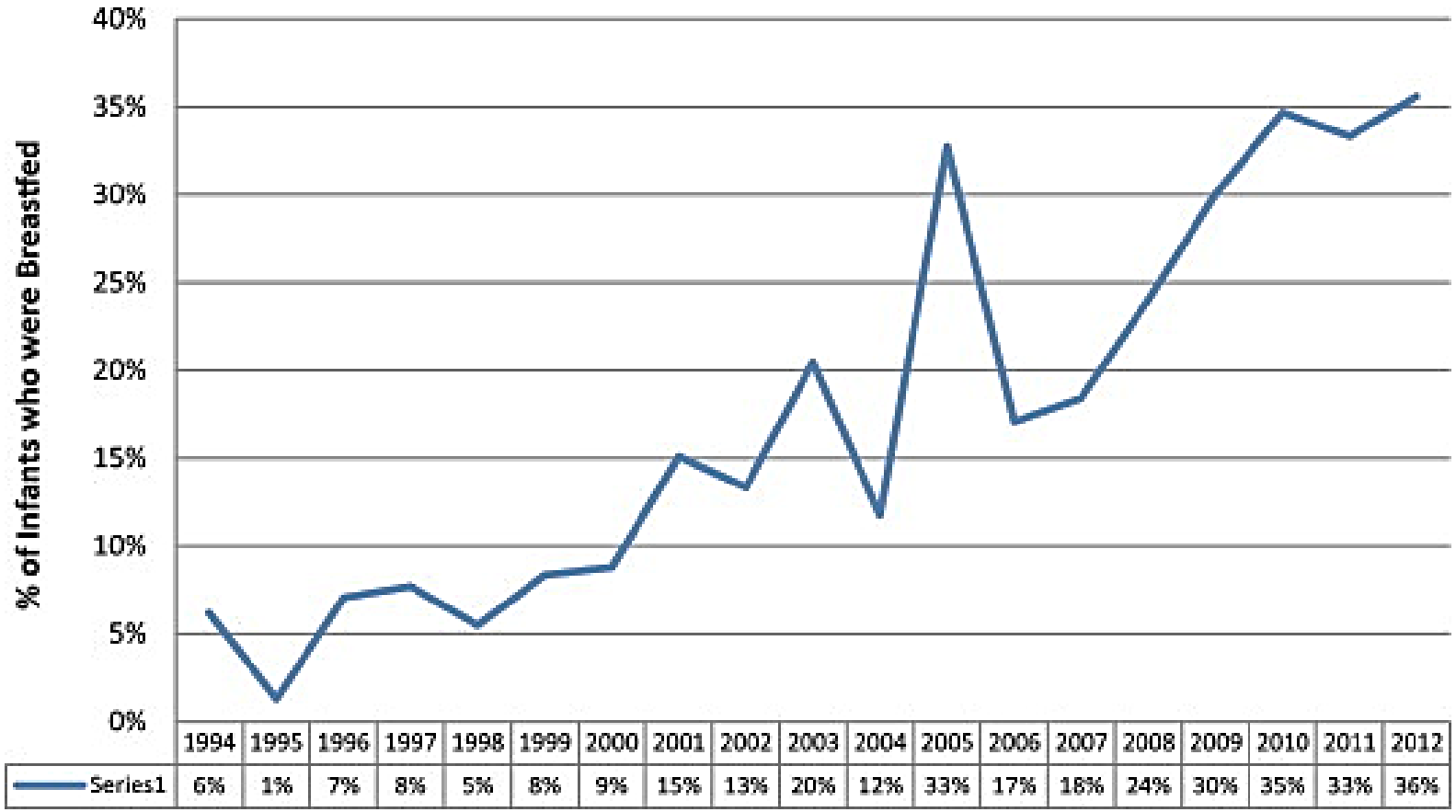

Fig. 1.

Breast-feeding Trends in Transplant Recipients Reporting to the NTPR.

National Transplantation Pregnancy Registry (NTPR), 2012

Transplantation and Pregnancy-Recommendations

- High-risk pregnancy
- **Good prognosis if:**
  - ✓ **1-2 years** waiting time posttransplant
  - ✓ Scr<1.5 mg/dl and stable
  - ✓ Normal blood pressure (target level?)
  - ✓ No proteinuria or minimal proteinuria (below 300-500 mg/d)
  - ✓ No recent acute rejection episode or UTI
  - ✓ Low-dose prednisone (≤7.5 mg/d)
  - ✓ No recent infections especially CMV-viral prophylaxis has been completed
  - ✓ Normal blood glucose level

Consensus Group Recommendations

- Counseling at the pretransplant evaluation and after transplantation
- Vaccination: pre-transplant or pre-pregnancy (influenza, Hepatitis B, tetanus)
- Follow-up with high-risk OB
- MMF **should be stopped at least 3 months before pregnancy; OK to switch to azathioprine**
- Close follow-up for acute rejection
- Frequent blood work for Cyclo/TAC level monitoring
- Good blood pressure and glucose control during pregnancy

Recommendations

- Treatment of anemia (OK to use EPO and iron) and UTIs
- Fetal surveillance: close follow-up
- C-section for usual indications
- **Breast-feeding**: controversial, not absolutely contraindicated, recent reports: most likely OK with TAC/Cyclo/AZA/Pred
- **Follow-up of offspring**: Long-term consequences of immunosuppressive agents?

Recommendations

Future research:

- Prospective observational studies and support of the current registries
- Other organ transplants-organ/recipient specific guidelines
- Impact of pregnancy on short and long-term graft function
- Target blood pressure and best BP meds to use
- The optimal immunosuppressive regimen during pregnancy and breast-feeding
- New immunosuppressive drugs and safety
- The long-term effects of immunos on the offspring

What Happened to Case #1?

- MMF was decreased and stopped over 1 month: started on azathioprine; the dose of tacrolimus was increased
- Spontaneous abortionx1
- First successful pregnancy (22 months posttransplant) and vaginal delivery-induction of labor at 36 weeks due to increased serum creatinine (2.0 mg/dl) and mild preeclampsia

Case #1

- Second pregnancy: vaginal delivery-complicated by postpartum bleeding with cervix and vaginal rupture, ex-lap, supracervical hysterectomy, repair of cervical and vaginal lacerations; 12 units PRBCs, 11 units of FFPs and platelets, 10 units of cryoprecipitate and AKI-recovered
- Scr 1.36 mg/dl on recent labs, on TAC/MMF and prednisone

Questions-Answers

- Is pregnancy advisable in transplant recipients? **YES in certain conditions and lots of counseling needed**
- Will pregnancy be complicated? **DEPENDS (Scr/HTN/proteinuria)**
- Will the baby be healthy? **YES**
- Will there be any long-term harm (mother and the baby)? **NO/BUT long-term studies still needed**

Review Paper

- **A best-practice position statement on pregnancy after kidney transplantation: focusing on the unsolved questions. The Kidney and Pregnancy Study Group of the Italian Society of Nephrology**

Cabiddu G, et al J Nephrol 2018