

**Pregnancy in Women with End
Stage Renal Disease**

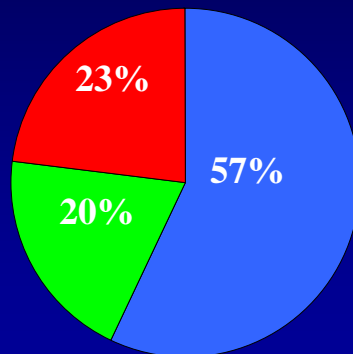
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**Will pregnancy lead to renal failure
in a woman with renal disease?**

Effect of Pregnancy on Renal Function

Women with Moderate Renal Insufficiency

57 Women 70 Pregnancies



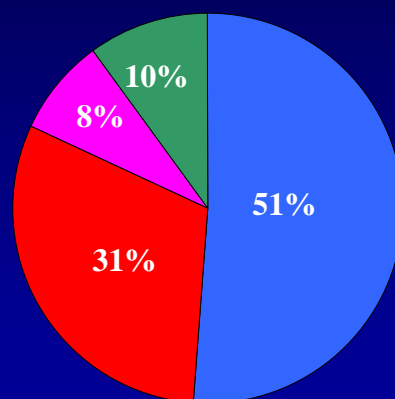
- Stable From Early Pregnancy to 6 weeks Post Partum
- Decline in Renal Function during Pregnancy
- Decline in Renal Function during 1st 6 weeks postpartum

Jones & Hayslett, 1996

Effect of Pregnancy on Renal Function

Women with Moderate Renal Insufficiency

57 women, 70 pregnancies



- Stable Renal Function From Early Pregnancy to 6 Months Post Partum
- Sustained pregnancy related decline in renal function
- Pregnancy Related Decline with Recovery
- Decline in Renal Function between 6 weeks and 6 months

Jones & Hayslett, 1996

Pregnancy Outcome in Moderate Renal Insufficiency

	Creatinine 1.4-2.4 mg/dl N=67	Creatinine \geq 2.5 mg/dl N=15
SI	61 (91%)	15 (100%)
SB4	4 (6%)	0
NND	2 (3%)	0
Premature	37 (55%)	11 (73%)
IUGR	31%	57%

Jones and Hayslett, 1996

Pregnancy in Moderate Renal Insufficiency: Update 2000-2010

18 pregnancies 15 women

- **Outcome**
 - Surviving infants 15 (83.3%)
 - Second Trimester SAB 3

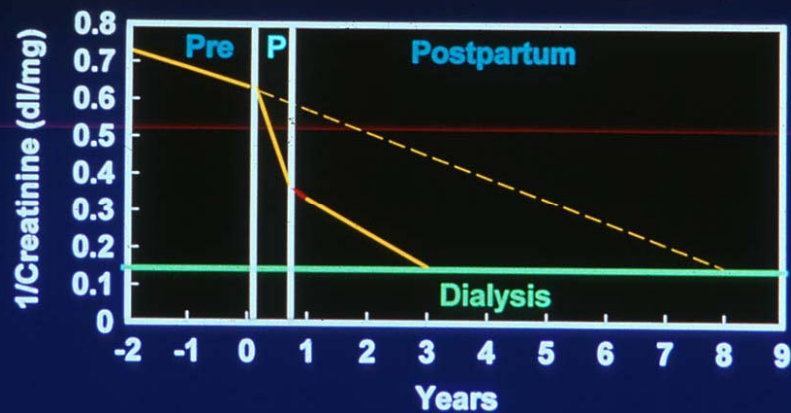
- **Renal Function**
 - Dialysis during pregnancy 3
 - Rapidly worse 5
 - Same 8
 - Better 1

• Loyola Data

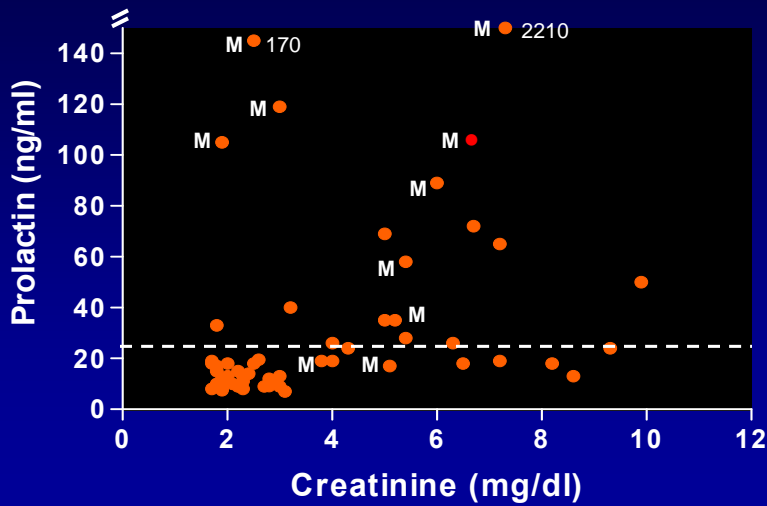
Creatinine > 4 mg/dl during Pregnancy

- 5 women
 - 3 dialysed. All infants survived
 - 2 not dialysed: second trimester spontaneous abortion

Extrapolation of 1/Cr to Time of Dialysis (Serum Cr = 8 mg/dl)



Prolactin Levels in Patients with Chronic Renal Insufficiency



M – Taking Medication

Hou et al., Am J Kidney Dis, 6:245, 1985

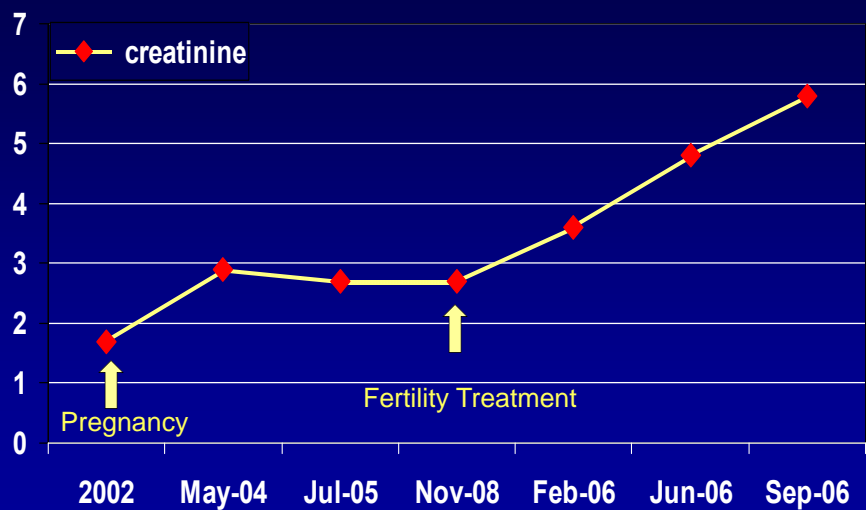
Fertility Treatment in CKD

- #1 IgA nephropathy. Creatinine 3.2 mg/dl progressed. Healthy twins by surrogate
- #2 IgA nephropathy: Creatinine 2.8 Few implantable embryos. No pregnancy
- #3 PKD. Creatinine 2. Non viable pregnancy. Creatinine increased to 2.3 mg/dl

Fertility Treatment in Women with Renal Insufficiency

- 43 year old woman with IgA nephropathy
- 1994 Diagnosis creatinine 1.2 mg/dl
- Prepregnancy: creatinine 1.7 mg/dl
- Post pregnancy: 2.7 mg/dl
- Pre fertility rx 2.7 mg/dl
- Post fertility re: progression to ESRD
- Currently pregnant post transplant

Creatinine during Fertility Treatment



Pregnancy in Woman Requiring Dialysis

Survey Results

- **Units Responding** 930
- **Women Aged 14-44** 6230
 - **Hemodialysis Patients** 4531
 - **Peritoneal Dialysis Patients** 1699
- **Total Pregnancies** 344

Frequency of Conception in Dialysis Patients

- Belgium 0.3%
- Japan 0.44%
- United States 0.5%
- Saudi Arabia 1%

Frequency of Conception

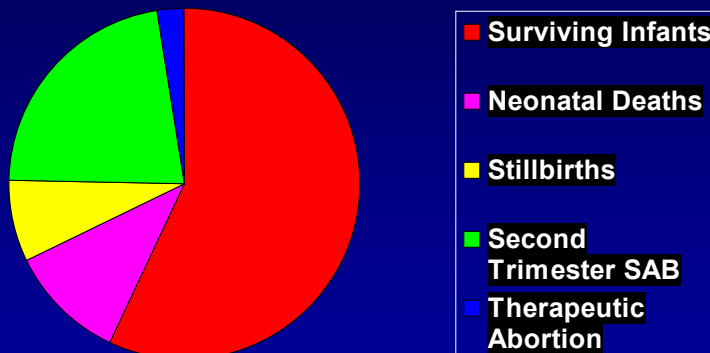
- Pregnancies 1992-1995 135 (2.2%)
 - Hemodialysis 109 (2.4%)
 - Peritoneal Dialysis 18 (1.1%)*

• *p<.01

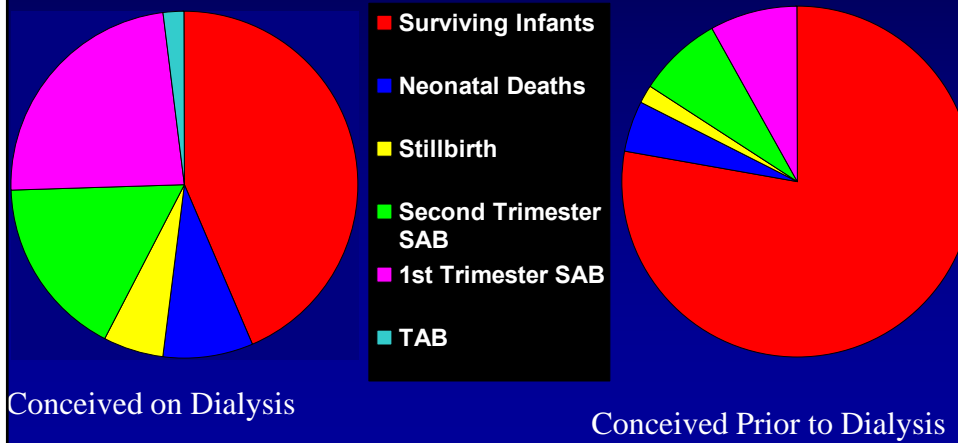
HCG β in a Dialysis Patient

• Wks Gestation	HCG	Normal
• 5 wks	13,270	75-2600
• 5 wks 3 days	30,323	850-20,800
• 5 wks 5 days	44,685	850-20,800
• 7 weeks	133,708	4000-100,200

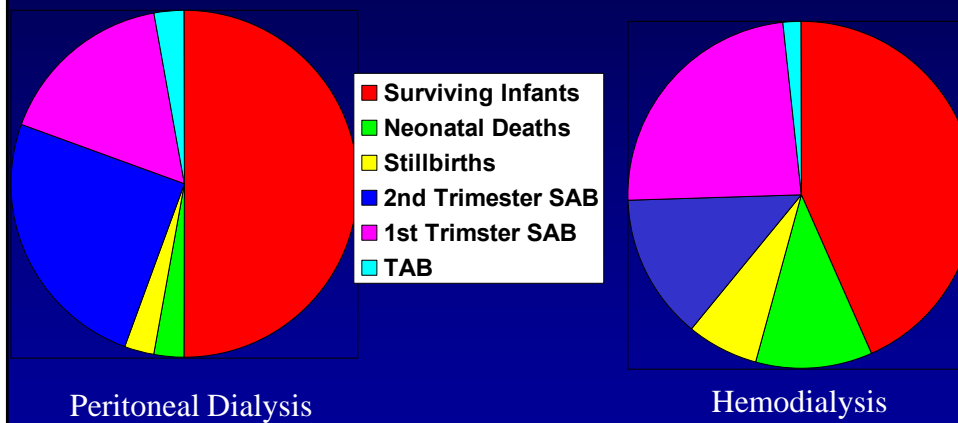
Outcome of Pregnancy in Women Treated with Dialysis Women who Conceived on Dialysis N=216



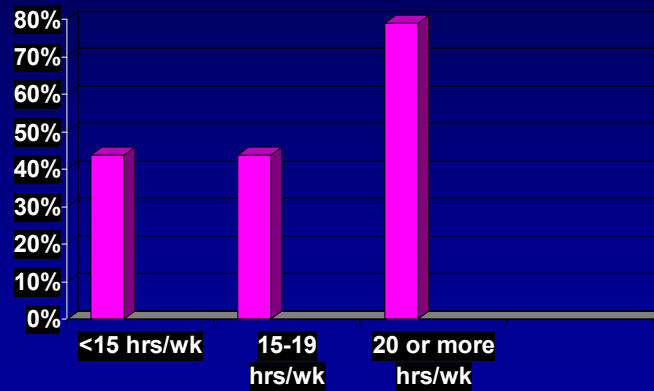
Outcome of Pregnancy in Women Treated with Dialysis



Outcome vs Dialysis Modality

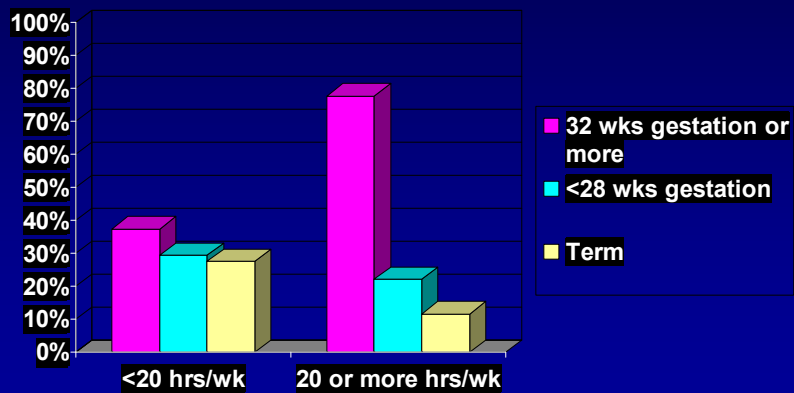


Infant Survival vs Intensity of Dialysis



P<.05

Prematurity vs Hours/WK of Dialysis



Pregnancy in Nocturnal Dialysis Patients

5 women 7 pregnancies

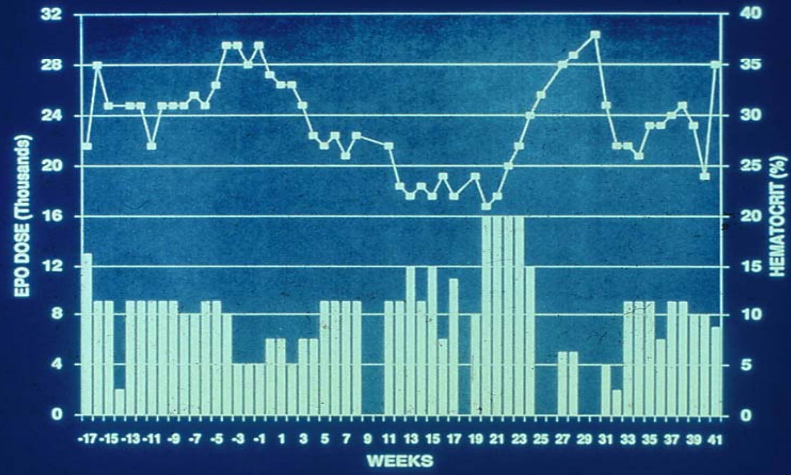
- 45 Women on Nocturnal Dialysis
 - 5 women conceived (15.6%)
 - Dialysis time Pre Pregnancy
 - 36 hrs/week
 - Dialysis time during Pregnancy
 - 48 hrs/wk
- Barua et al. CJASN 3:392-396,2008

Pregnancy in Nocturnal Dialysis Patients

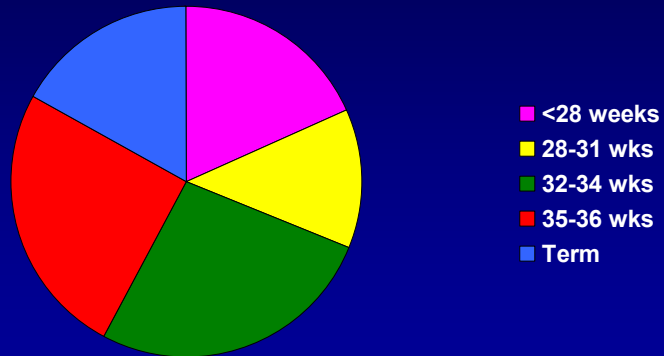
5 women 7 pregnancies

- Outcome
 - 6 surviving infants
 - 1 elective abortion
 - Birthweight
 - 1 < 1500 g
 - 1 > 1500 g < 2500 g
 - 4 > 2500g
 - Gestational Age
 - 1 30 weeks
 - 5 > 36 wks
- Barua et al. CJASN 3:392-396,2008

Erythropoietin Dose and Hematocrit in a Pregnant Dialysis Patient



Gestational Age of Infants Born to Dialysis Patients



Pregnancy in Renal Transplant Recipients

Guidelines for Counseling Transplant Recipients about Pregnancy

- More than 1 year post transplant
- Serum creatinine \leq 1.5 mg/dl
- No rejection within a year
- Hypertension controlled
- Glucose controlled

Outcome of Pregnancy in Transplant Recipients

**National Transplant Pregnancy Registry
262 women, 384 Pregnancies, 395 Outcomes**

- | | |
|-------------------------|-----------|
| • Surviving Infants | 332 (84%) |
| • Neonatal Deaths | 6 (1.5%) |
| • Stillbirths | 12 (3%) |
| • Spontaneous Abortions | 40 (10%) |
| • Ectopic | 5 (1.3%) |

Outcome of Pregnancy in Transplant Recipients 42 Pregnancies 27 Women

- **Surviving Infants 35 (83.3%)**
- **Neonatal Deaths 2 (4.76%)**
- **Ectopic Pregnancies 2 (4.76%)**
- **Spontaneous Abortion 1 (2.38%)**
- **Therapeutic Abortion 1(2.38%)**
- **Still Pregnant 1 (2.38%)**

• Data from Loyola and Rush

Maternal Problems in Pregnant Transplant Recipients

- **Urinary Tract Infections (40%)**
- **Preeclampsia (30%)**
- **Decreased Renal Function (10%)**
- **Increased Proteinuria (40%)**
- **Rh Sensitization**

Effect of Pregnancy on Graft Survival

	Creatinine Start	Creatinine Follow-up	Graft Survival Follow-up
Pregnant Patients N=18	1.3 mg/dl	1.4 mg/dl	77.8%
Female	1.3 mg/dl	1.4 mg/dl	69.2%
Controls N=26			
Male	1.3 mg/dl	1.3 mg/dl	69.6%
Controls N=23			

First et al, 1995

Graft and Patient Survival 2 months to 25 yrs Follow-up N=27

- Alive with functioning graft 17
- Alive with a new graft 3
- On dialysis 3
- Died 2
- Lost to Follow-up 2

• Data from Loyola and Rush

Prednisone in Pregnancy

Pregnancy Category B

Maternal Effects

Hypertension
Poor Wound Healing
Glucose Intolerance
Adrenal Insufficiency
↑ Infection
Uterine Rupture ?

Fetal Effects

No ↑ Birth Defects
Lymphopenia
Thymic Hypoplasia
Adrenal Insufficiency
↑ Infection

Cyclosporine: Outcomes

• Neoral		• Sandimmune	
• Live births	80%	• Live Births	76%
• SAB	18%	• SAB	12%
• TAB	2%	• TAB	8%
• Stillborn	1%	• Stillborn	3%
• Ectopic	0%	• Ectopic	1%

Cyclosporine: Outcomes

- | | | | |
|------------------------|--|------------------------|--|
| • Neoral | | • Sandimmune | |
| • Mean Birth Wt 2416 g | | • Mean Birth wt 2493 g | |
| • Mean Gest Age 36 wks | | • Mean Gest Age 36 wks | |
| • Premature 56% | | • Premature 52% | |
| • Low Birth Wt 54% | | • Low Birth Wt 45% | |

Birth Defects in Cyclosporine Treated Patients

- Not clear cut pattern
- Higher than the general population (4.97%)
- Number of diabetic patients unknown

Tacrolimus

Pregnancy Category C

30 recipients 38 pregnancies

- **Maternal Complications**
 - Hypertension 47%
 - Diabetes 13%
 - Infection 35%
 - Rejection 14%

Tacrolimus (Outcomes)

- **39 Outcomes**
 - Live Birth 74%
 - SAB 21%
 - TAB 3%
 - Stillborn 3%
 - Premature 57%
 - Low Birth wt 66%

Tacrolimus in Pregnancy N = 27

- Mean Birthweight 2638 \pm 781 g
- Mean Gestational Age 36.6 \pm 3 wks
- K \geq 6 mEq/L (4-10.9) 8/11 (73%)
- Creatinine \geq 1.2 mg/dl (0.8-3.2) 3/7 (43%)

Mycophenolate Mofetil in Pregnancy

- Embryotoxic in Animals
- 33 Pregnancies in 24 solid organ transplant recipients NTPR data base
- 18 Live births
- 15 spontaneous abortions
- 4 with Congenital anomalies
- Sifontis et al. Transplantation 82: 1698-1702, 2006 (NTPR data)

Congenital Anomalies with MMF

- Microtia
- Cleft Lip
- Hypoplastic nails
- Multiple Malformations
- Hypoplastic nails
- Shortened Fifth Finger
- Anencephaly

Azathioprine in Pregnancy

Pregnancy Category D

- No activation by the Fetal Liver
- No ↑ Congenital Anomalies
- Fetal Neutropenia
- ↑ Childhood Cancers ?
- ↓ Fertility in offspring?

Sirolimus

- 7 pregnancies in NTPR
- 4 Live Births
- 3 Spontaneous abortions
- 1 Congenital anomalies (also on MMF)

Decreased Ferility in Men on Sirolimus

Sirolimus

- Sperm Count: 28.6 million
- Motile sperm: 22.2%
- Pregnancies/1000 pt yrs: 5.9

Other

- Sperm Count: 292.2 million
- Motile sperm: 41%
- Pregnancies/1000 pt yrs: 92.9
- Anglicheau et al. Am J Transplant 8:1471-1479, 2008

Sirolimus

- **Male infertility may not be reversible**
- **mTOR may play a role in implantation of the embryo (in women)**

Drug Changes Prior to Pregnancy

- **Stop Statins: cholesterol will rise during pregnancy**
- **Change MMF to azathioprine**
- **Change sirolimus to calcineurin inhibitor**
- **Stop Ace inhibitors**

Infections in Pregnant Transplant Recipients

- **Urinary Tract Infection 40%**
- **CMV**
- **Herpes**
- **Toxoplasmosis**
- **Listeria**

Follow-up on Children of Cyclosporine Treated Mothers

- **N = 175 from 133 Mothers**
- **16% had developmental delay**

• **Stanley et al., 1999 NTPR data**

Conclusions

- **A 30-50% of women who become pregnant with renal insufficiency have acceleration of disease.**
- **80-100% of pregnancies result in surviving infants.**
- **Start Dialysis at creatinine of 4 mg/dl**

Conclusions

- **Pregnancy is safe in most transplant recipients with good kidney function**
- **Cyclosporine is not a prenatal vitamin but MMF is teratogenic.**

Acknowledgements

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