Pregnancy and Renal Disease

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Case One

A 28 year-old G0,P0 consults you about risks involved in becoming pregnant. She has IgA nephropathy diagnosed by renal biopsy at age 14. She complains of swelling in her ankles at the end of the day. She has proteinuria and creatinine has gradually increased. She is taking lisinopril 20 mg daily but uses no NSAIDS. Her blood pressure is 152/100 and she has 1+ pretibial edema.

Case One (cont.)

The urine dipstick reveals 3+ protein and 3+ heme; microscopically she has 5-12 RBC/HPF, mostly acanthocytes.

BUN 31 mg/dl; creatinine 2.1 mg/dl; albumin 4.2 mg/dl, Hb 12.4

Urine protein/creatinine ratio 2.4

Fundamental Issues

- What is the impact of pregnancy on renal function in patients with underlying renal disease or impaired renal function?
- What is the impact of underlying renal disease or impaired renal function on pregnancy?

Data Are Limited

- No randomized clinical trials, no meta-anaylses
  - Difficult to identify appropriate controls
- Primarily small series
  - Usually only one or a few collaborative centers
  - Absence of uniform data points; limited # data points
  - Variable, often limited, post-partum follow-up
- Difficulty distinguishing whether acceleration of renal insufficiency during or right after pregnancy is due to pregnancy or natural history of renal disease.

Impact of Pregnancy on Renal Disease/Renal Insufficiency

- Depends mostly on severity of underlying renal disease at onset of pregnancy
- Depends in part on whether hypertension controlled during pregnancy
  - Whether severe preeclampsia occurs
- Less dependant on type of renal disease
  - Some small series suggest MPGN and FSGS important
  - Diabetes may exacerbate proteinuria and hypertension
  - Lupus nephritis--advise delaying pregnancy until disease inactive ≥ 6 months to avoid pregnancy flare

Normal Renal Function at Baseline (With or Without Renal Disease)

- Creatinine tends to decrease first half of pregnancy (due to increased GFR)
- Baseline proteinuria (if present) tends to increase

Mild Renal Insufficiency (Creatinine ≤ 1.4 mg/dl)

- Data from several small series with mild renal insufficiency at baseline: Minimal to no impact of pregnancy in terms of acceleration renal insufficiency.

Moderate to Severe Renal Insufficiency Creatinine ≥ 1.4 mg/dl

- Largest Series: 82 pregnancies in 67 women with creatinine ≥ 1.4 at conception (mean creatinine 1.9)
  - Mean creatinine increased to 2.5 by 3rd trimester
  - 20% had worse renal function during pregnancy
  - 23% had worse renal function by 6 wks postpartum
    - 8% recovered; 10% declined further
    - 8 women (10%) → ESRD within year of pregnancy
- Creatinine >2.0 outset: Highest likelihood decline (33% had accelerated decline renal function)

Jones DC, Hayslett JP. N Engl J Med 1996;335:226-32

Impact of Renal Disease on Pregnancy Outcomes

- Fetal Survival Good (70 to 100%)
  - Lower with uncontrolled hypertension
    - Especially with MAB > 105 start of conception
- Risk of Prematurity estimated 45 -70%
- Risk of Intrauterine Growth Restriction estimated 20-50%
- Risk of Preeclampsia increased
  - Greater risk of occurrence during second trimester
  - Associated with both prematurity and intrauterine growth restriction

Case Two

A 41 y.o. nulliparous woman who underwent in-vitro fertility is now pregnant with twins. She has enjoyed good health but is obese and has a 20-year smoking history. The first half of pregnancy has been uneventful. At 32 ½ weeks she is hypertensive (145/98) and has proteinuria (urine protein/creatinine ratio 1.7). Five days later she complains of persistent, severe headache and right upper quadrant abdominal pain. The blood pressure is 165/108. Platelet count is 70, creatinine 1.3, AST 94, and ALT 92.

Preeclampsia

- Systemic disorder unique to pregnancy marked by new onset hypertension and proteinuria after 20 weeks gestation
- Eclampsia: onset of seizures in preeclampsia
- Preeclampsia may be superimposed on chronic hypertension in pregnancy
- Incidence is 3-14% pregnancies worldwide

Risk Factors

- First pregnancy, past history preeclampsia, family history preeclampsia, multiple gestation, obesity, pre-gestational diabetes, pre-existing renal disease, pre-existing hypertension, advanced materna age, antiphospholipid antibody syndrome.
    - Cigarette smokers have lower risk preeclampsia nonsmakers

Preeclampsia Prevention

- No clearly established preventive measures
  - Some data (very small studies) suggest possible benefit of low-dose aspirin in prevention in high risk groups
    - But weight of evidence not strong
  - No benefit from calcium supplementation

Other Forms Hypertension in Pregnancy

- Chronic hypertension: Antedates pregnancy (systolic ≥ 140 and diastolic ≥ 90 mmHg)
  - Limited data regarding degree of hypertension to treat and target goals
    - Expert opinion: treat bp > 155-165/95-100 mmHg
    - Aim for lower levels if end-organ damage present
- Gestational hypertension: mild hypertension latter half pregnancy (but no proteinuria or other signs preeclampsia)

Antihypertensive Drugs in Pregnancy

- Drugs of choice:
  - Methyldopa: nearly 50 years experience; excellent long-term safety profile in pregancy
  - Labetalol: both alpha and beta-adrenergic blocking properties; may have less impact on uterine/placental blood flow
  - Nifedipine (long-acting): appears safe
    - Less data on Diltiazem and Verapamil but likely safe
    - May worsen hypotension and neuromuscular blockade if magnesium sulfate used for preeclampsia

Antihypertensive Drugs in Pregnancy

- Drugs to avoid:
  - ACE inhibitors and ARBs
    - First trimester exposure: higher risk major congenital malformations, esp. cardiovascular and cns malformations
    - Later pregnancy exposure: oligohydramnios, hypocalvaria
- Drugs to use with caution:
  - Diuretics: avoid volume depletion
  - Beta blockers: may ↓ uterine/placental blood flow; may be linked to intrauterine growth restriction and fetal bradycardia

Case Three

A 28 year-old woman who underwent a deceased donor renal transplant 26 months ago is now 6 weeks pregnant (unplanned pregnancy). She has CKD due to focal segmental glomerulosclerosis. Her immunosuppressive medications include prednisone, tacrolimus and mycophenolate mofetil. She is not hypertensive. The creatinine is 1.2 mg/dl and the urine protein/creatinine ratio is 0.8.

Pregnancy in Recipients of Renal Transplants

- Transplantation restores fertility
- Advise waiting 1 year (living related donor) or 2 years (deceased donor) after transplant
  - AST advises waiting one year if renal function stable/no rejection
  - Reduced risk rejection/lower doses prednisone required
- Risk pregnancy-related renal function worsening depends on degree renal impairment at outset
  - Data suggests no long-term impact pregnancy on graft function
- Risk of prematurity and intrauterine growth restriction > 50 %
- Risk Preeclampsia about 30 %

Pregnancy in Recipients of Renal Transplants

- Safety of immunosuppressive drug use in pregnancy not clearly established
  - Some drugs appear safer than others
- Azathioprine and low-dose prednisone
  - Minimal adverse effects on fetus
- Calcineurin Inhibitors
  - Monitor levels carefully to prevent toxicity
- Avoid sirolimus and mycophenolate mofetil
  - FDA medwatch warning for mycophenolate

Pregnancy and Renal Disease: Conclusions

- Likelihood of pregnancy-related worsening of renal function depends on degree of impairment at outset of pregnancy
- Fetal survival very good with renal disease but risk of prematurity and intrauterine growth restriction increased
- Preeclampsia risk increased with renal disease
  - Monitor closely for possible onset in 3rd trimester
- Fertility restored by transplantation
- Know which antihypertensives and immunosuppressive medications to use or to avoid in pregnancy