

# **Pregnancy and kidney disease**

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# INTRODUCTION

Pregnancy is characterized by a myriad of physiologic changes, of which the emergence of a placenta and growing fetus are the most dramatic.

Early in pregnancy, (SVR) decreases and arterial compliance increases. These changes are evident by 6 weeks gestation.

| <b>Variable</b>  | <b>Change in Pregnancy</b>  |
|--|---|
| <b>Hemodynamic Parameters</b>                          |   |
| Plasma volume  | Increases 30%–50% above baseline  |
| Blood pressure   | Decreases by approximately 10 mm Hg below prepregnancy level, with nadir in second trimester; gradual increase toward prepregnancy levels by term |
| Cardiac output   | Increases 30%–50%   |
| Heart rate   | Increases by 15–20 beats/min  |
| Renal blood flow                                       | Increases to 80% above baseline   |
| Glomerular filtration rate                             | 150–200 mL/min (increases to 40%–50% above baseline)  |
| <b>Serum Chemistry and Hematologic Changes</b>         |   |
| Hemoglobin   | Decreases by an average of 2 g/L (from 13 to 11 g/L) owing to plasma volume expansion out of proportion to the increase in red blood cell mass    |
| Creatinine   | Decreases to 0.4–0.5 mg/dL  |
| Uric acid  | Decreases to a nadir of 2.0–3.0 mg/dL by 22–24 weeks, then increases back to nonpregnant levels toward term                                       |
| pH   | Increases slightly to 7.44  |
| Partial pressure of carbon dioxide (pCO <sub>2</sub> ) | Decreases by approximately 10 mm Hg to an average of 27–32 mm Hg  |
| Calcium  | Increased calcitriol stimulates increases in both intestinal calcium reabsorption and urinary calcium excretion                                   |
| Sodium   | Decreases by 4–5 mEq/L below nonpregnancy levels  |
| Osmolality   | Decreases to a new osmotic set point of approximately 270 mOsm/kg   |

# RENAL ADAPTATION TO PREGNANCY

- In pregnancy, the kidney length increases by 1–1.5 cm and kidney volume increases by up to 30%.
- There is physiologic dilatation of the urinary collecting system in approximately 50% of pregnant women, more frequently on the right than the left

The increased proteinuria in pregnancy:

- Increased GFR
- Increased permeability of the glomerular basement membrane
- Reduced tubular reabsorption of filtered protein.



# RESPIRATORY ALKALOSIS OF PREGNANCY

Minute ventilation begins to rise by the end of the first trimester, and continues to increase until term.

Progesterone mediates this response by direct stimulation of respiratory drive and by increasing sensitivity of the respiratory center to CO<sub>2</sub>.

This results in a mild respiratory alkalosis, pressure of carbon dioxide (pCO<sub>2</sub>) falls to approximately 27–32 mm Hg.

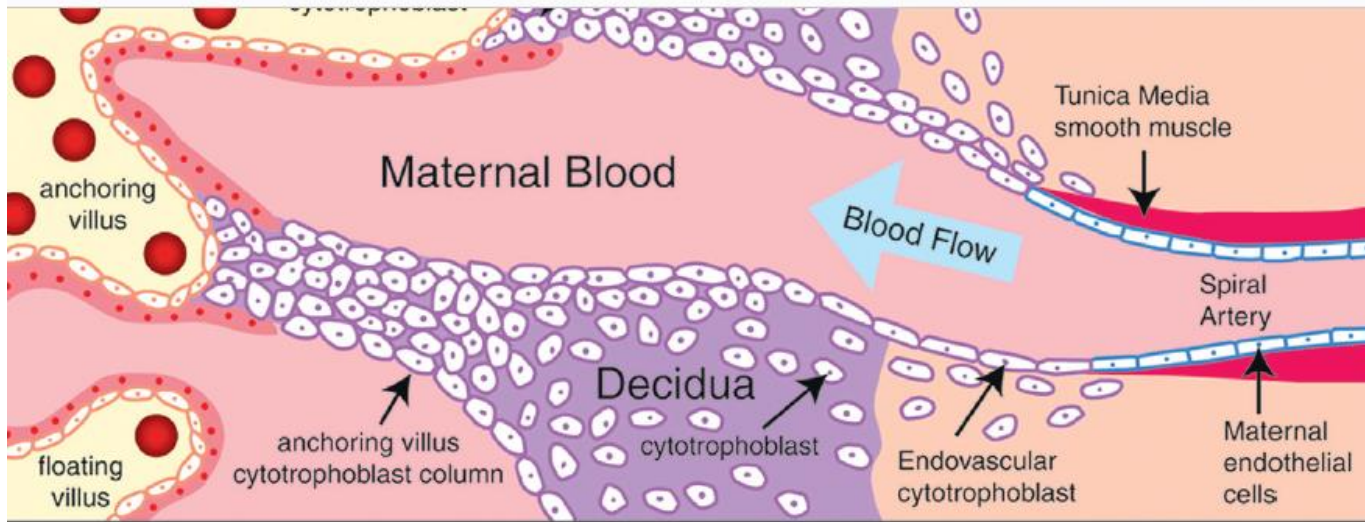
# DIABETES INSIPIDUS OF PREGNANCY

Circulating levels of vasopressinase, an enzyme that hydrolyzes arginine vasopressin, are increased during normal pregnancy.

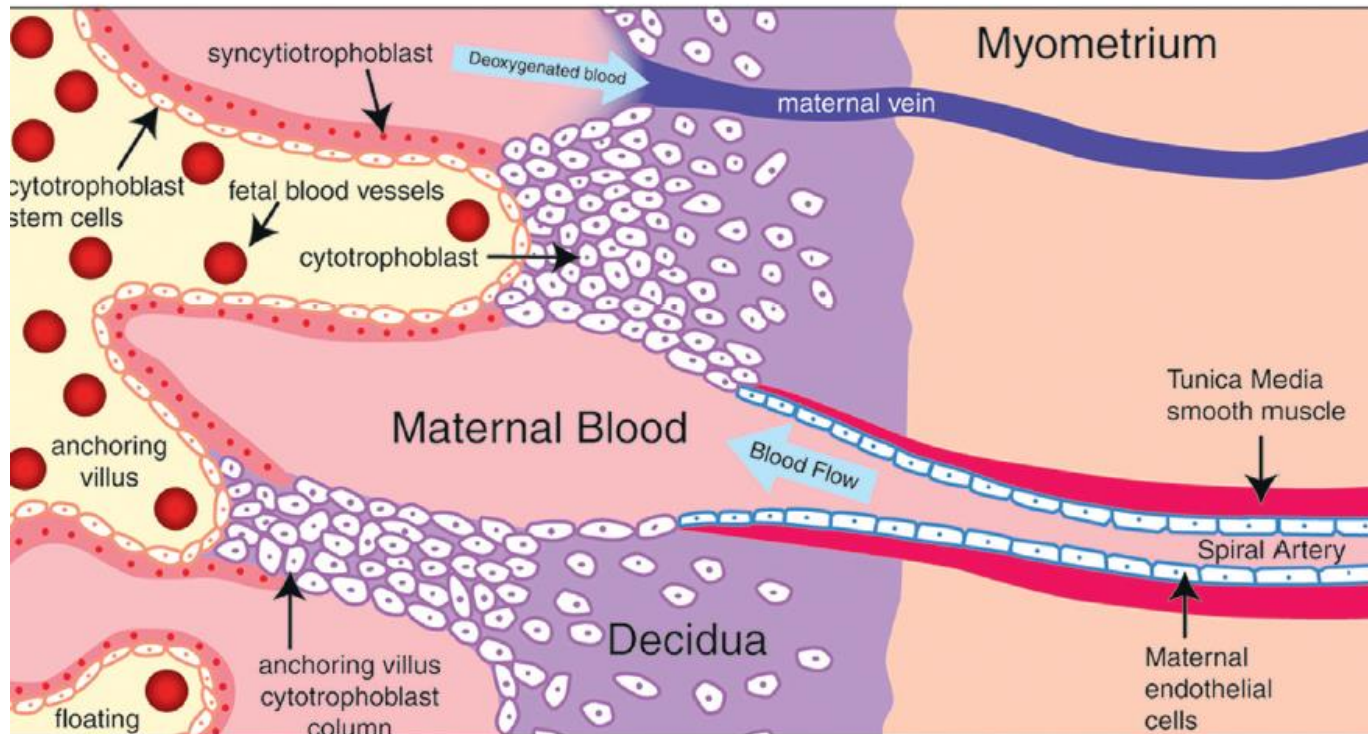
This syndrome of transient diabetes insipidus presents during the second trimester and disappears after delivery.

It is important to recognize this entity because affected women may become dangerously hypernatremic, especially with cesarean section using general anesthesia and/or water restriction in the delivery room.





### Preeclampsia



# PREECLAMPSIA AND HELLP SYNDROME

Preeclampsia affects approximately 5% of pregnancies worldwide.

The diagnosis of preeclampsia required the new onset of both hypertension and proteinuria after 20 weeks' gestation.

The diagnosis of preeclampsia in women with chronic hypertension and/or underlying proteinuric renal disease on clinical criteria alone remains challenging.

| <b>Risk Factor</b>  | <b>Pooled Relative Risk<br/>(95% CI)</b> |
|---|--|
| Antiphospholipid antibody syndrome  | 2.8 (1.8–4.3) <sup>44</sup>              |
| Chronic kidney disease  | 1.8 (1.5–2.1) <sup>44</sup>              |
| Prior preeclampsia  | 8.4 (7.1–9.9) <sup>44</sup>              |
| Nulliparity   | 2.1 (1.9–2.4) <sup>44</sup>              |
| Chronic hypertension  | 5.1 (4.0–6.5) <sup>44</sup>              |
| Pregestational diabetes mellitus  | 3.7 (3.1–4.3) <sup>44</sup>              |
| Multiple gestations   | 2.9 (2.6–3.1) <sup>44</sup>              |
| Strong family history of<br>cardiovascular disease (heart<br>disease/stroke in two or more<br>first-degree relatives) | 3.2 (1.4–7.7) <sup>474</sup>             |
| Systemic lupus erythematosus  | 2.5 (1.0–6.3) <sup>44</sup>              |
| Obesity (prepregnancy BMI > 30 kg/<br>m <sup>2</sup> )  | 2.8 (2.6–3.1) <sup>44</sup>              |
| Family history of preeclampsia  | 2.4 (1.8–3.6) <sup>41</sup>              |
| Advanced maternal age (>40 years)   | 1.5 (1.2–2.0) <sup>44</sup>              |
| Excessive gestational weight gain<br>(>35 lbs)  | 1.9 (1.7–2.0) <sup>273</sup>             |
| Assisted reproductive technology  | 1.8 (1.6–2.1) <sup>44</sup>              |
| Previous episode of acute kidney<br>injury  | 5.9 (3.6–9.7) <sup>475</sup>             |

## Diagnostic Criteria for Preeclampsia

|                             |   |
|-----------------------------|---|
| Hypertension                | <p>≥140 mm Hg systolic or ≥90 mm Hg diastolic after 20 weeks of gestation on two occasions at least 4 hours apart in a woman with a previously normal blood pressure</p> <p>OR</p> <p>With blood pressures ≥160 mm Hg systolic or ≥105 mm Hg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy</p> |
| <i>AND</i>                  |   |
| Proteinuria                 | <p>≥300 mg/24 h (or this amount extrapolated from a timed collection)</p> <p>OR</p> <p>Protein-to-creatinine ratio ≥ 0.3 mg protein/mg creatinine</p> <p>OR</p> <p>Dipstick 2+ (used only if other quantitative methods not available)</p> <p><i>OR in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:</i></p>             |
| Thrombocytopenia            | ≤100,000 platelets/mL   |
| Renal insufficiency         | Serum creatinine concentrations >1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease  |
| Impaired liver function     | Elevated blood concentrations of liver transaminases to twice normal  |
| Pulmonary edema             |   |
| Cerebral or visual symptoms |   |

# URIC ACID

Serum uric acid is elevated in most women with preeclampsia primarily as a result of enhanced tubular urate reabsorption.

Serum uric acid levels are correlated with the presence and severity of preeclampsia and with adverse pregnancy outcomes, even in gestational hypertension without proteinuria.

# Continue...

In such patients, a serum uric acid level  $>5.5$  mg/ dL in the presence of stable renal function might suggest superimposed preeclampsia.

# CLINICAL FEATURES OF SEVERE PREECLAMPSIA

- Oliguria (<500 mL urine in 24 hours)
- Acute kidney injury (AKI), though uncommon
- Persistent headache or visual disturbances
- Seizures
- Pulmonary edema complicates 2%–3% of severe preeclampsia

# ECLAMPSIA

Although eclampsia most often occurs in the setting of hypertension it can occur without these warning signs.

Radiologic imaging by (MRI) is usually not indicated when the diagnosis is apparent, but typically shows vasogenic edema, predominantly in the subcortical white matter of the parietooccipital lobes

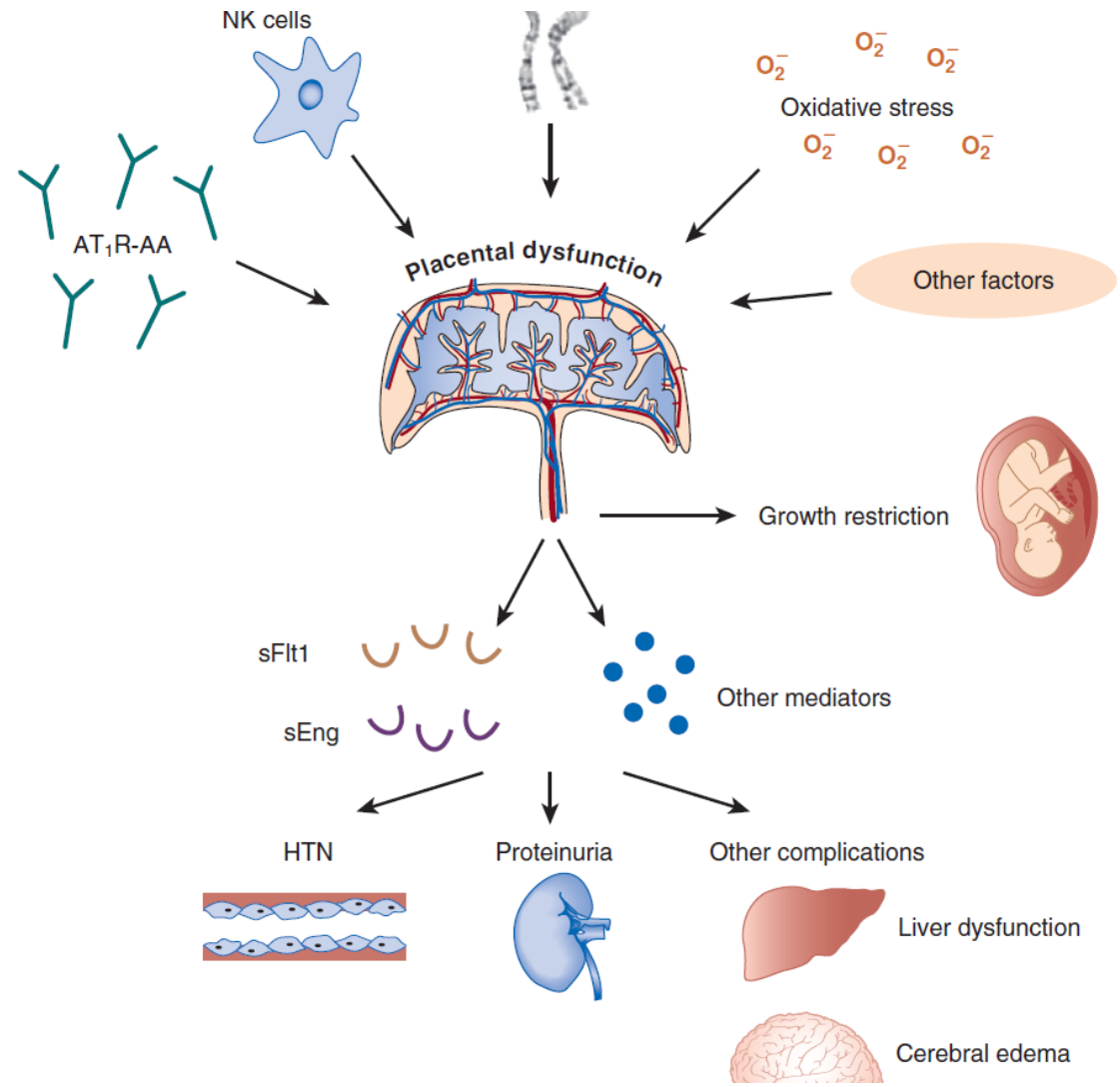


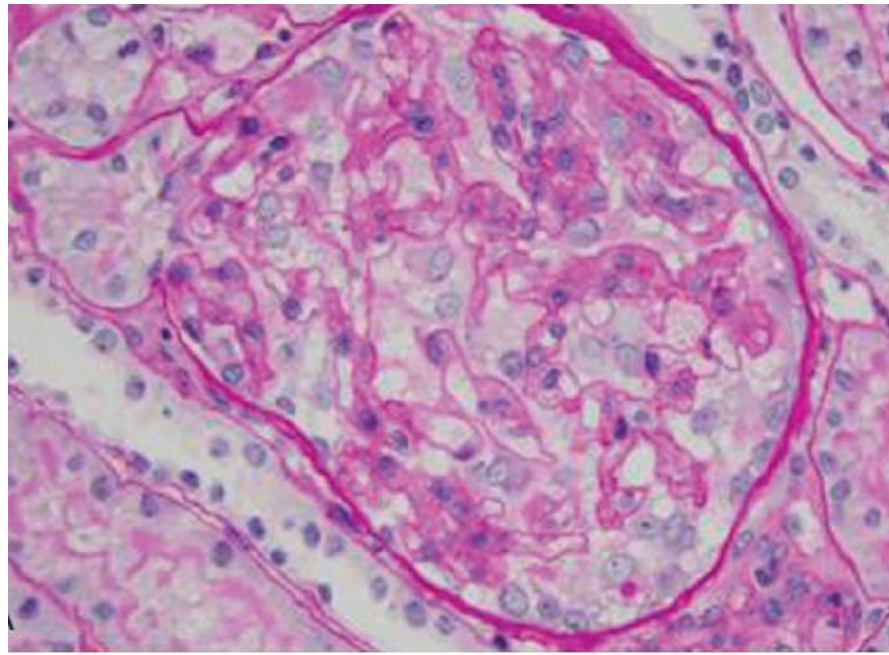
# HELLP SYNDROME

HELLP is the syndrome of hemolytic anemia, elevated liver enzymes, and low platelets.

The HELLP syndrome is a severe form of preeclampsia, which can occur in the absence of proteinuria.

|                                 | <b>HUS/TTP</b>  | <b>HELLP</b>              | <b>AFLP</b>               |
|---------------------------------|-----------------|---------------------------|---------------------------|
| <b>Clinical Characteristic:</b> |                 |                           |                           |
| Hemolytic anemia                | +++             | ++                        | ±                         |
| Thrombocytopenia                | +++             | ++                        | ±                         |
| Coagulopathy                    | -               | ±                         | +                         |
| CNS symptoms                    | ++              | ±                         | ±                         |
| Renal failure                   | +++             | +                         | ++                        |
| Hypertension                    | ±               | +++                       | ±                         |
| Proteinuria                     | ±               | ++                        | ±                         |
| Elevated AST                    | ±               | ++                        | +++                       |
| Elevated bilirubin              | ++              | +                         | +++                       |
| Anemia                          | ++              | +                         | ±                         |
| Ammonia                         | Normal          | Normal                    | High                      |
| Effect of delivery on disease   | None            | Recovery                  | Recovery                  |
| Management                      | Plasma exchange | Supportive care, delivery | Supportive care, delivery |





Glomerular  
endotheliosis

# SCREENING

Risk assessment early in pregnancy is important to identify those who require close monitoring after 20 weeks.

Higher BP in the first or second trimesters, even in the absence of overt hypertension, is associated with elevated risk for preeclampsia in healthy nulliparous women.

# Clinical Relevance

Preeclampsia is characterized by marked alterations in angiogenic factors.

- Measurement of maternal serum sFlt1
- placental growth factor (PlGF)
- The sFlt1-to- PlGF ratio may inform diagnosis and risk stratification in women with suspected preeclampsia.

# PREVENTION OF PREECLAMPSIA

- ANTIPLATELET AGENT
- CALCIUM FOR THE PREVENTION OF PREECLAMPSIA
- ANTIOXIDANTS AND NUTRITIONAL INTERVENTION
- SLOW-MOLECULAR-WEIGHT HEPARIN

# Chips:

Control of Hypertension in Pregnancy Study trial showed:

That treatment of hypertension in pregnancy to a “tight” blood pressure target (DBP 85 mm Hg), as compared with a “less-tight” target (DBP 100 mm Hg), was safe, with no significant differences in the rate of pregnancy loss

Women treated to the tight blood pressure target had a significantly lower rate of maternal complications, including severe hypertension, thrombocytopenia, and transaminitis with symptoms.



| <b>First-Line Agents</b>                       |   |  |
|--|---|--|
| <b>Oral</b>                                    |   |  |
| Methyldopa<br>Labetalol                        | First line; extensive safety data<br>Preferred over other $\beta$ -blockers owing to theoretical beneficial effect of $\alpha$ -blockade on uteroplacental blood flow | Short duration of action/multiple daily dosing<br>Short duration of action/multiple daily dosing. May exacerbate reactive airway disease |
| Long-acting nifedipine                         | Once-daily dosing (slow-release preparation)  | Edema  |
| <b>Intravenous</b>                             |   |  |
| Labetalol<br>Nicardipine                       | Good safety data<br>Extensive safety data on use as a tocolytic during labor; effective   |  |
| <b>Second-Line Agents</b>                      |   |  |
| Hydralazine                                    | Extensive clinical experience   | Increased risk of maternal hypotension and placental abruption when used acutely   |
| Metoprolol                                     | Potential for once-daily dosing using long-acting formulation   | Safety data less extensive than for labetalol  |
| Verapamil, diltiazem                           | No evidence of adverse fetal effects  | Limited data   |
| <b>Generally Avoided</b>                       |   |  |
| Diuretics                                      | No evidence of adverse fetal effects  | Theoretically may impair pregnancy-associated expansion in plasma volume   |
| Atenolol<br>Nitroprusside                      |   | May impair fetal growth<br>Risk of fetal cyanide poisoning if used for >4 hours  |
| <b>Contraindicated</b>                         |   |  |
| Angiotensin-converting enzyme (ACE) inhibitors |   | Multiple fetal anomalies; see text   |
| Angiotensin receptor antagonists               |   | Similar risks as ACE inhibitors  |

# ANTIHYPERTENSIVE DRUGS IN BREASTFEEDING

- ❑  $\beta$ -Blockers with high protein binding, such as labetalol and propranolol, are preferred over atenolol and metoprolol, which are concentrated in breast milk.
- ❑ Diuretics may decrease milk production and should be avoided.
- ❑ ACE inhibitors are poorly excreted in breast milk and generally considered safe in lactating women. Enalapril and captopril are preferred in lactating women.

# OBSTRUCTIVE UROPATHY AND NEPHROLITHIASIS

- ❖ Calcium oxalate and calcium phosphate constitute the majority of the stones produced during pregnancy
- ❖ Ultrasonography and MRI are the preferred methods to exclude obstruction and visualize stones.
- ❖ Lithotripsy is relatively contraindicated during pregnancy due to its adverse effects on the fetus.
- ❖ However, extracorporeal shock wave lithotripsy has been used during the first 4–8 weeks of pregnancy without known adverse consequences to the fetus.

# KIDNEY BIOPSY IN PREGNANCY

- Indications for kidney biopsy during pregnancy are similar to those in the nonpregnant population.
- However, most complications were minor but this is a period of uncertain fetal viability should complications require preterm delivery, kidney biopsy should be avoided between 23 and 26 weeks gestation.

| <b>Drug</b>                          | <b>Recommendations</b>   |
|--------------------------------------|--|
| Prednisone                           | Safe when used long term at low to moderate doses (5–10 mg/day)<br>Safe when given acutely at high doses for treatment of acute rejection  |
| Cyclosporine                         | Extensive clinical data suggest safe at low-to-moderate clinical doses<br>Changes in absorption and metabolism require close monitoring of levels and frequent dose adjustments in pregnancy |
| Tacrolimus                           | Similar to those for cyclosporine, although somewhat less data available   |
| Sirolimus                            | Embryo/fetal toxicity in rodents was manifested as mortality and reduced fetal weights (with associated delays in skeletal ossification); human studies are lacking                          |
| Azathioprine                         | Considered safe at dosages < 2 mg/kg per day, but at higher doses associated with fetal growth restriction   |
| Mycophenolate mofetil                | Contraindicated in pregnancy (teratogenic in animal and human studies)   |
| Muromonab-CD3 (OKT-3)                | Case reports of successful use for induction in unsuspected pregnancy and for acute rejection, but data are limited  |
| Antithymocyte globulin (C)           | Animal studies have not been reported, and there are no controlled data from use in human pregnancy  |
| Belatacept, basiliximab, alemtuzumab | Avoid in pregnancy; inadequate safety data in humans   |

# Acute Kidney Injury in Pregnancy

- The main cause of AKI in developing countries is severe sepsis from septic abortions.
- Causes of AKI also include hypertensive disorders and sepsis, as well as thrombotic microangiopathy, heart failure, acute fatty liver and post-partum hemorrhage.
- Hyperemesis gravidarum in the first trimester can lead to volume depletion that can require hospitalization and IV fluid replacement
- Increased risk of cortical necrosis in pregnancy may be due to the hypercoagulable nature of pregnancy.

# Continue...

- The criteria for the diagnosis of AKI in pregnancy have not been standardized.
- An increase in Scr of 0.3 mg/dl, consistent with stage 1 in the AKIN, may represent a significant kidney injury.

# Diabetic Nephropathy

- Diabetic nephropathy is characterized by a slowly progressive course, with the gradual development of hypertension, albuminuria, and loss of GFR.
- Diabetic nephropathy is present in 6% of pregnant women with type 1 DM.
- The risk for deterioration in renal function is highest in women with a Scr > 1.4 mg/dl.

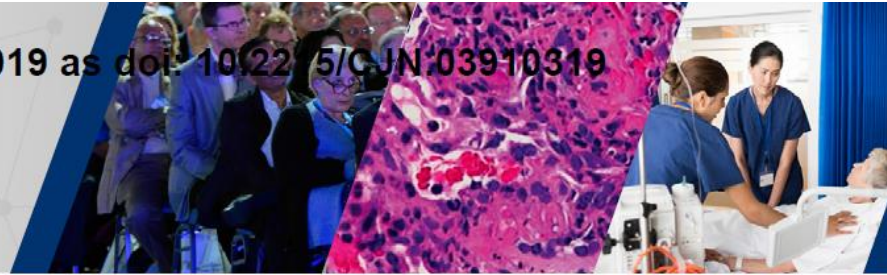


# Continue...

- The risk for deterioration in renal function and progression to ESRD is highest in women with a Scr > 1.4 mg/dl.
- ACE inhibitors and ARBs are contraindicated in pregnancy, but 3–6 months of therapy prior to conceiving may have renal protective effects.
- Women with type 1 DM are at an increased risk of preeclampsia.

# Chronic Kidney Disease in Pregnancy

- Women with antepartum Scr of  $> 2.0$  mg/dl were at particularly high risk of losing renal function as a consequence of pregnancy.
- Women with milder CKD (Scr  $< 1.4$  mg/dL) may expect to have good maternal and fetal outcomes.
- While women with advanced disease (Scr  $1.4$ – $2.9$  mg/dL), are at a high risk for pregnancy complications.
- Women with Scr values  $\geq 3.0$  mg/dL may permanently lose renal function with pregnancy.



## Pregnancy in a Kidney Transplant Patient

Song C. Ong and Vineeta Kumar

CJASN 14: ●●●–●●●, 2019. doi: <https://doi.org/10.2215/CJN.03910319>

### Introduction

In 1958, Edith Helm, who received a kidney from her identical twin sister, became the first woman to successfully give birth after transplantation. Many women have since followed in her footsteps. In this “How I Treat” article, we review our approach to treating a patient from preconception counseling to postpartum care.

### Patient

contrasted with Medicare claims data that show a lower post-transplant live birth rate of 55.4% and a lower pregnancy rate than in the general population (7).

The KDIGO and the European Best Practices guidelines advise delaying pregnancy until after the first and second year post-transplantation, respectively (8,9). Predictors of good maternal and fetal outcomes include a younger maternal age, stable graft function with no recent episodes of graft rejection, serum creatinine level of <1.5 mg/dl, proteinuria of <500 mg a day, and normal or well controlled hypertension (4–6,8).

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# Continue...

The KDIGO and the European Best Practices guidelines advise delaying pregnancy until after the first and second year post-transplantation.

Patients are seen at 1–2 monthly intervals and referred to a high-risk obstetrics clinic.

We perform laboratory work to follow kidney function and drug levels every 4 weeks in early pregnancy, increasing in frequency to every 2 weeks in the second and third trimesters.

# Continue...

MMF is a teratogen and is substituted with azathioprine at least 6 weeks before attempting pregnancy.

The kidney allograft does not affect normal vaginal delivery and a cesarean section is not routinely indicated.

The online LACTMED database maintained by the National Institutes of Health is a helpful resource on the safety of drugs during breast feeding.

# Continue...

Rates of graft loss at 2 years post-transplant vary from 5% to 9%.

Trimethoprim- sulfamethoxazole and atorvastatin were stopped.

As a result of changes in GFR and drug metabolism, drug levels can vary during pregnancy.

To maintain whole blood drug levels of tacrolimus in their prepregnancy range necessitates a 20%–25% increase in total dose.



# Renal stones in pregnancy

Shireen Meher, Norma Gibbons and Ranan DasGupta

## Abstract

Diagnosis and treatment of renal stones during pregnancy is a complex problem. Risks to the fetus from ionising radiation and interventional procedures need to be balanced with optimising clinical care for the mother. Management of such patients requires a clear understanding of available options, with a multidisciplinary team approach. In this review, we discuss the role of different diagnostic tests including ultrasound, magnetic resonance urography, and computerized tomography. We also provide an update on recent developments in the treatment of renal stones during pregnancy. Expectant management remains first-line treatment. Where definitive treatment of the stone is required, new evidence suggests that ureteroscopic stone removal may be equally safe, and possibly better than traditional temporising procedures.

## Keywords

Renal stones, urolithiasis, nephrolithiasis, pregnancy

## Introduction

Renal stones are relatively rare during pregnancy. However, they are a common cause of non-obstetric abdominal pain in pregnant women. Management of renal stones in pregnancy is challenging. It can be difficult to differentiate between physiological and pathological

particularly in women. However, nephrolithiasis is relatively more common in men.<sup>15</sup> Risk factors include a positive family history, dietary factors such as low intake of water or increased intake of animal protein and sodium, environment factors such as hot climate, and underlying medical conditions such as hyperparathyroidism.<sup>15,16</sup>

The incidence of renal stones in pregnancy is quoted to be 1 in 1500,

# Management

In pregnancy, 64–84% stones have been reported to be passed spontaneously with conservative therapy, and 50% of those that are not passed during pregnancy may be passed after delivery.

Opioids are generally prescribed to treat acute renal colic and may be used safely in pregnancy

NSAIDS they are generally avoided in pregnancy due to risk of adverse effects on the fetal kidney, oligohydramnios, and premature closure of ductus arteriosus.



# Continue...

URS may be considered as first-line treatment unless there are clear indications for a temporising treatment with a ureteral stent or PCN.



## Prepregnancy counselling and management of pregnancy in haemodialysis patients

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Pregnancy in patients on dialysis carries major risks for both the mother and the foetus/neonate. Ideally, if the personal situation, maternal age and all other factors allow waiting long enough, then pregnancy should be postponed until after kidney transplantation, because the overall risks are reduced. Waiting is not an option when maternal age is too advanced, when we

100 mL (urea <17 mmol/L) is related to a birthweight >1500 g and a gestational age at birth >32 weeks [4]. Frequent and short home haemodialysis often does not provide enough dialysis time and should be limited to women with residual kidney function. The haemodialysis prescription must include a minimum of 20 h depending on the residual kidney function, and

Ideally, if the personal situation, maternal age and all other factors allow waiting long enough, then pregnancy should be postponed until after kidney transplantation, because the overall risks are reduced.

- limits to pregnancy is altered fertility in these women resulting from:  
lack of normal oestrogen and progesterone synthesis,
- Anovulatory cycles
- low luteinizing hormone and follicle-stimulating hormone levels
- High prolactin level

# Goals:

Calcium inhibitors such as nifedipine and other drugs such as labetalol and methyldopa to reach arterial pressure targets  $<140/90$ mmHg.

Cinacalcet is contraindicated in this situation.

In case of active immune disease, patients should be counselled against pregnancy.

Diabetes should be closely monitored to reach HbA1c  $<7\%$  without hypoglycaemia.

# Continue:

- All pregnancy outcomes benefit from long and daily haemodialysis.
- A pre-dialysis blood urea nitrogen level  $<50\text{mg}/(\text{urea } <17\text{mmol/L})$  is related to a birthweight  $>1500\text{ g}$  and a gestational age at birth  $>32\text{week}$
- The haemodialysis prescription must include a minimum of 20 h depending on the residual kidney function, and with new guidelines, increasing to 36 h/week for women with no residual kidney function.

## goals:

The goal for pre-dialysis urea should be as low as 10 to a maximum of 15mmol/L after the day without dialysis.

The dry weight should be regularly re-evaluated with an increase of 1 kg/month in order to maintain an arterial pressure <140/90mmHg without per-dialysis arterial hypotension.

Protein intake should be increased from 1.5 to 1.8 g/kg/day.

First trimester screening for aneuploidy should be standard, but pregnancy associated plasma protein A is increased in haemodialysis patients and can be less sensitive to detect genetic trouble

- Its increase is correlated with parathyroid hormone
- Acidosis
- Dialysis vintage and is enhanced after the heparin injection

Ultrasonography should be repeated in the second trimester, at 20 WG

Magnesium sulphate is contraindicated for (GFR) <30mL/min, and its use should prompt a check of the magnesium level.

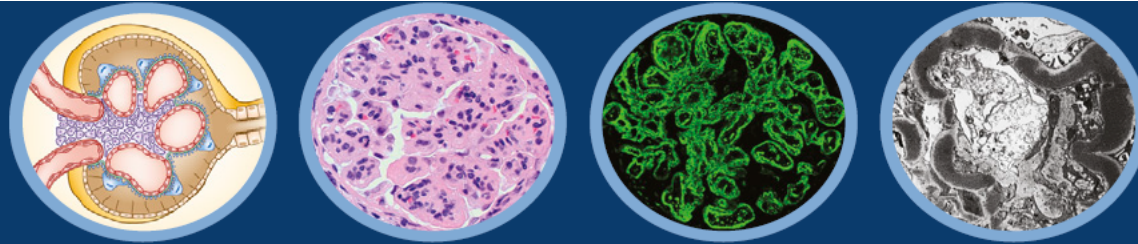
Tranexamic acid half-life increases to 18 h in dialysis patients versus 2 h in patients with normal kidney function and therefore must be used at a lower dose.

Breastfeeding is negatively impacted by ultrafiltration but is not  
Contraindicated.

Some ACE inhibitor, such as captopril, enalapril and quinalapril, can be used.



# Glomerular Disease



## Pregnancy and Glomerular Disease A Systematic Review of the Literature with Management Guidelines

Kimberly Blom,<sup>\*</sup> Ayodele Odutayo,<sup>\*</sup> Kate Bramham,<sup>†</sup> and Michelle A. Hladunewich<sup>\*</sup>

### Abstract

During pregnancy, CKD increases both maternal and fetal risk. Adverse maternal outcomes include progression of underlying renal dysfunction, worsening of urine protein, and hypertension, whereas adverse fetal outcomes include fetal loss, intrauterine growth restriction, and preterm delivery. As such, pregnancy in young women with CKD is anxiety provoking for both the patient and the clinician providing care, and because the heterogeneous group of glomerular diseases often affects young women, this is an area of heightened concern. In this invited review, we discuss pregnancy outcomes in young women with glomerular diseases. We have performed a systematic review in attempt to better understand these outcomes among young women with primary GN, we review the studies of pregnancy outcomes in lupus nephritis, and finally, we provide a potential construct for management. Although it is safe to say that the vast majority of young women with glomerular disease will have a live birth, the counseling that we can provide with respect to individualized risk remains imprecise in primary GN because the existing literature is extremely dated, and all management principles are extrapolated primarily from studies in lupus nephritis and diabetes. A search of pregnancy outcomes and management strategies in these

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# Systematic Review of Primary Glomerular Diseases

- The most commonly reported GN was IgA nephropathy, with 12 studies including 10–136 patients.
- In the second largest study of 118 pregnant women with hypertension at baseline (BP140/90 mmHg) or impaired renal function (eGFR,70 ml/min per 1.73 m<sup>2</sup>) were more likely to have an unsuccessful pregnancy.
- Only four studies reported outcomes for women with FSGS), all were published before 1990.

Only two studies included women with minimal change or membranous nephropathy.

Maternal renal flares in women with lupus nephritis, include severity of preexisting disease, nonwhite, presence of anticardiolipin antibody or lupus anticoagulant, and hypertension.

Hydroxychloroquine is recommended to be commenced or continued for all women with lupus nephritis because cohort studies have shown maternal and fetal benefits.

# Immunosuppression

Prednisone is metabolized by placental 11- $\beta$ -hydroxysteroid dehydrogenase.

Type 2 to inactive cortisone However, dexamethasone, is not inactivated, and the fetus is exposed to 30% of the maternal dose.

Stress doses of glucocorticoids (typically hydrocortisone) are recommended during labor for women taking the equivalent of prednisone 20 mg or more for >3 weeks.

Azathioprine requires activation by inosinate pyrophosphorylase to metabolite 6-mercaptopurine, which is absent in the fetal liver.

Cyclophosphamide and mycophenolate mofetil are teratogenic.

Cyclophosphamide is associated with calvaria, ear and craniofacial structure, limb and visceral organ abnormalities, developmental delay with first trimester exposure and growth restriction, suppression of hematopoiesis, and neurologic impairment.

# Rituximab

In our practice, we consider rituximab only as a last resort in early pregnancy pending further data. Neonatal monitoring is recommended before routine vaccination, with delay if necessary.

# Management of Worsening Proteinuria

- GN can present or flare during pregnancy, and at least early on in pregnancy.
- The diagnostic approach is similar to the nonpregnant state, including a careful urinalysis and the relevant serologic assessment.
- M-type phospholipase A2 receptor in membranous nephropathy and soluble urokinase plasminogen activator receptor in FSGS

In lupus and vasculitis, serology can often assist with diagnosis, rendering biopsy less necessary.

However, the presentation of de novo significant proteinuria or nephrotic syndrome early in pregnancy typically does necessitate a renal biopsy to establish a diagnosis and guide immunosuppressive therapy.

In patients in whom renal biopsy has been delayed to the postpartum period, it is ideal to wait 4–6 weeks for resolution of potential coexisting endotheliosis.



After a diagnosis is established, immunosuppressive treatment should begin promptly.

pulse methylprednisolone and plasmapheresis are options that can be applied for a more rapid effect where appropriate.

Conservative treatments include compression stockings and avoidance of prolonged standing.

Loop diuretics are appropriate for severe edema, and supportive albumin infusions have been reported in case reports of women with severe nephrosis.

# Thromboprophylaxis:

women with severe proteinuria and serum albumin  $< 20$  g/L should receive thromboprophylaxis throughout pregnancy.

Continued for at least 6 weeks, because the postpartum period carries a particularly high risk of thrombosis.

# Nephrotic syndrome in pregnancy

- Clinical features

the baseline characteristics of the 26 pregnancies with NS

All 19 subjects underwent kidney biopsy

NS was a new diagnosis during pregnancy in 12 of the 26 women, 8 of whom underwent renal biopsy during pregnancy and 4 after delivery.

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# Management

- Of the 26 pregnancies, 7 women received prednisone, with a daily total dose of 60 to 120 mg.
- Of the 7 women who received prednisone, 6 were initiated based on the findings of the kidney biopsy, and 1 was empirically treated with steroids.
- One patient with known C3 glomerulopathy received eculizumab during pregnancy.

## Table 2 | Kidney biopsy diagnosis

| Pathologic diagnosis ( <i>N</i> = 19)    | No. (%) |
|--|---------|
| Focal segmental glomerulosclerosis       | 8 (42)  |
| IgA nephropathy                          | 3 (16)  |
| Membranous nephropathy                   | 3 (16)  |
| Fibrillary glomerulonephritis            | 1 (5)   |
| Membranoproliferative glomerulonephritis | 1 (5)   |
| C3 glomerulonephritis                    | 1 (5)   |
| Minimal change disease                   | 1 (5)   |

### Risk factors for adverse maternal and fetal outcomes

| Variable                                 | OR (95% CI); <i>P</i> value           |                                       |  |
|--|---------------------------------------|---------------------------------------|--|
|  | Preeclampsia                          | Low birth weight                      | Preterm delivery                       |
| History of hypertension                  | 3.75 (0.77–18.21);<br><i>P</i> = 0.10 | 3.75 (0.77–18.21);<br><i>P</i> = 0.10 | 3.33 (0.68–16.30);<br><i>P</i> = 0.14  |
| Maternal age at presentation             | 0.98 (0.87–1.11);<br><i>P</i> = 0.70  | 0.98 (0.87–1.11)<br><i>P</i> = 0.77   | 0.98 (0.88–1.10)<br><i>P</i> = 0.75    |
| Serum creatinine at presentation         | 2.45 (0.11–55.13);<br><i>P</i> = 0.57 | 2.45 (0.11–55.13);<br><i>P</i> = 0.57 | 9.20 (0.35–238.69);<br><i>P</i> = 0.18 |
| Peak creatinine during pregnancy         | 3.00 (0.73–12.27);<br><i>P</i> = 0.13 | 3.00 (0.73–12.27);<br><i>P</i> = 0.13 | 4.04 (0.61–26.80);<br><i>P</i> = 0.15  |
| Serum albumin                            | 0.47 (0.14–1.61);<br><i>P</i> = 0.23  | 0.47 (0.14–1.61);<br><i>P</i> = 0.23  | 0.40 (0.12–1.32);<br><i>P</i> = 0.13   |
| Proteinuria at presentation              | 1.26 (1.03–1.53);<br><i>P</i> = 0.02  | 1.26 (1.03–1.53);<br><i>P</i> = 0.02  | 1.28 (1.00–1.64);<br><i>P</i> = 0.051  |
| Peak proteinuria during pregnancy        | 1.19 (1.02–1.40);<br><i>P</i> = 0.03  | 1.19 (1.02–1.40);<br><i>P</i> = 0.03  | 1.22 (1.00–1.48);<br><i>P</i> = 0.045  |
| Systolic blood pressure at presentation  | 1.02 (0.98–1.06);<br><i>P</i> = 0.30  | 1.02 (0.98–1.06);<br><i>P</i> = 0.30  | 1.03 (0.98–1.08);<br><i>P</i> = 0.25   |
| Diastolic blood pressure at presentation | 1.03 (0.96–1.10);<br><i>P</i> = 0.41  | 1.03 (0.96–1.10);<br><i>P</i> = 0.41  | 1.09 (1.00–1.18);<br><i>P</i> = 0.054  |

# DISCUSSION

- In our study, the mean age of gestation at presentation was 18.6 weeks, consistent with previous observation that proteinuria.
- Before 20 weeks gestation is suggestive of primary kidney disease rather than preeclampsia.
- Only those who underwent a kidney biopsy were included the renal pathology and exclude preeclampsia as the primary cause of NS.

# Conclusions

Contrary to previous studies that reported good maternal-fetal outcomes in pregnant women with NS and relatively preserved renal function, we have shown a high incidence of both maternal and fetal complications in this population that correlate with the degree of proteinuria.

In the future, we look toward better and larger trials to assess the impact of interventions for hypertension, preeclampsia, and primary kidney disease in pregnant women.



*Thank  
you*

