



Pregnancy and Rheumatology disease

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PUBLIC HEALTH

RECOMMENDATIONS

**PREGNANCY IN INFLAMMATORY RHEUMATIC DISEASES: PATIENT
AND HEALTH PROFESSIONAL PERSPECTIVES**

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IRDS

Inflammatory rheumatic diseases are chronic ,systemic conditions that may affect women of reproductive age

- Rheumatoid arthritis(RA)
- Systemic lupus erythematosus(SLE)
- Ankylosing spondylitis(AS)
- Psoriatic arthritis(PsA)
- Other IRDs require complex management during pregnancy due to disease activity



Continue.....

Studies indicate that pregnancy rates are **significantly lower** in this group compared to the general population

Insufficient knowledge about

- Disease activity
- Medication safety
- Breastfeeding often leads to unnecessary medication discontinuation
- Uncontrolled disease
- Pregnancy complications

Effective patient education should go beyond information transfer to address misconceptions, support shared decision-making, and encourage active patient participation in disease management

Optimal management of pregnant patients

- optimal management of pregnant patients with IRDs requires a rheumatologist-led multidisciplinary team
- Effective care depends on **coordination** among obstetricians, perinatologists, nephrologists , cardiologists, neonatologists, and clinical pharmacologists .
- In high-risk pregnancies, patient safety is compromised without clear team leadership and regular multidisciplinary assessments



Patient perspective

PUBLIC HEALTH

RECOMMENDATIONS

PREGNANCY IN INFLAMMATORY RHEUMATIC DISEASES: PATIENT
AND HEALTH PROFESSIONAL PERSPECTIVES

- For women with IRDs, pregnancy represents both a medical process and a significant emotional milestone, often marked by anxiety and uncertain their approach to pregnancy changes considerably after diagnosis, as physical limitations, medication concerns, and interactions with the healthcare system strongly influence their decisions
- Understanding the patient perspective is essential for clinicians to provide empathetic, effective, and sustainable care

Concerns:

- studies indicate that many women with IRDs voluntarily choose not to pursue pregnancy or parenting
 - This decision is often influenced by concerns about :
 - Medication effects on the fetus
 - Risk of disease flare-ups during pregnancy
 - Uncertainty about managing childcare with the disease
- Patients often feel isolated in their decision-making because of insufficient or conflicting information from healthcare professionals.
- often contribute to anxiety and depressive symptoms during pregnancy

Continue.....

- As a result, many patients **stop** their medication without consulting their physician, which can reactivate disease and harm both maternal and fetal outcomes
- Patients should receive clear, evidence-based, and personalized information that stopping medication without proper guidance may pose greater risks than the medication itself

Obstetrics and gynecology perspective

- The disease's unique pathophysiology, the effects of medications on the placenta and fetus, and the interaction between systemic inflammation and pregnancy complications



Obstetric risk assessment

- Should start before pregnancy
- Preeclampsia, gestational hypertension, intrauterine growth restriction, preterm birth, spontaneous abortion, and cesarean section occur **more frequently** in patients with IRDs than in the general population .
- The extent of these risks depends on disease type, pre-pregnancy disease activity, organ involvement, and the drug regimen used .
- Patients who conceive with active disease face a **higher risk** of adverse pregnancy outcomes than those in remission.
- Obstetric evaluation should therefore include both routine pregnancy monitoring and a systematic review of **disease-specific** risk factors

Continue....

- Delivery planning for patients with IRDs should involve a multidisciplinary team
- When deciding on the timing and method of delivery, consider disease activity, joint involvement, medications, thrombosis risk, and previous pregnancy complications.
- For patients on long-term corticosteroids, assess the need for stress dose steroids during the peripartum period, notify the anesthesia team in advance, and arrange a neonatology consultation to ensure safety .
- **Cesarean section** should be performed **only** for obstetric indications; rheumatic disease alone should not increase cesarean rates without thorough clinical evaluation

The postpartum period

- Is a critical yet often overlooked phase in managing patients with IRDs
- Sudden immunological and hormonal changes, along with treatment adjustments during pregnancy, significantly **increase** the risk of disease exacerbation
- Key management components include reorganizing breastfeeding and medication adherence, providing thromboembolism prophylaxis, and conducting psychosocial assessments
- The obstetrician's active involvement in postpartum follow-up, particularly during the high-risk first **six weeks**, is essential for early detection of maternal complications

Rheumatology perspective

- Teratogenic agents, including methotrexate and leflunomide, should be discontinued at **least 3 to 6 months** prior to conception, with a washout protocol recommended for leflunomide
- Although **hydroxychloroquine and sulfasalazine** are generally considered compatible with pregnancy
- Tumor necrosis factor (TNF) inhibitors require **re-evaluation** during the third trimester due to the potential for placental transfer and subsequent neonatal immunosuppression
- Assessment of ovarian reserve is particularly important in patients previously exposed to **cyclophosphamide**; measurement of anti-Müllerian hormone (AMH) levels and antral follicle count are critical components of this evaluation.
- In cases of diminished ovarian reserve, fertility-preserving strategies should be discussed in collaboration with reproductive medicine specialists
- As IRDs can independently reduce ovarian reserve and increase the risk of premature ovarian failure, routine pre-pregnancy evaluation should include ovarian reserve assessment **for all women with IRDs**

Artificial intelligence in pregnancy planning

- (AI) and machine learning are increasingly important in managing rheumatic diseases, particularly for decision support in complex high-risk scenarios such as pregnancy planning

In pregnant women with IRDs, the need to assess:

- Disease activity
- Drug exposure
- Ovarian reserve
- Comorbidities, and obstetric risks highlights where AI can add significant value.



 Preconception  During pregnancy	
 Patient tasks Counseling Education Adherence    	
● Attend preconception counseling ● Discuss family planning with physician ● Disclose all medications and concerns ● Complete infection screening tests ● Engage in shared decision-making	● Attend all rheumatology and obstetric visits ● Maintain medication; do not self-discontinue ● Report new or worsening symptoms promptly ● Participate in trimester-specific physical therapy ● Discuss delivery plan and postpartum care
 Specialist tasks Medication Screening Monitoring    	
● Assess disease activity; target remission ● Discontinue MTX/LEF $\geq$ 3–6 months prior ● Assess ovarian reserve (AMH, antral follicle count) ● Screen for latent TB, hepatitis B/C, HIV, rubella ● Optimize CV risk, osteoporosis, glycemic control ● Prescribe rehabilitation plan	● Monitor disease activity (validated tools) ● Review medication safety per trimester ● Re-evaluate TNF inhibitors in 3rd trimester ● Fetal ultrasound and Doppler monitoring ● Coordinate multidisciplinary team ● Plan delivery, peripartum steroids, postpartum monitoring

Management of Pregnancy in Rheumatic Disease

**EDITOR'S
PICK**

The Editor's Pick is the review paper by Maguire et al. Managing patients with rheumatic musculoskeletal disorders (RMD) during pregnancy and the postpartum period is challenging. Disease activity in some RMDs, such as rheumatoid arthritis, improve during the course of pregnancy and in others, such as systemic lupus erythematosus, it worsens. Then there is the issue of drug treatment during pregnancy to maintain remission and the potential undesirable effects on the fetus. This complex subject area is reviewed as well as the current American College of Rheumatology (ACR) guidelines on pregnancy and RMDs.

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Positive Impact	Negative Impact
Pregnancy planning and counselling	Active disease§
Disease remission*	End-organ damage:
Known autoantibody status	• Lupus nephritis • Pulmonary hypertension • Restrictive lung disease
Medication adherence	Unplanned pregnancy
Use of pregnancy-safe medications†	Unplanned cessation of treatment**
Close monitoring of disease activity‡	
Optimisation of general health	

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Relative contraindications	Absolute contraindications
Severe SLE flare within the past 6 months*	Advanced pulmonary hypertension
Stroke in the past 6 months	End-stage renal disease
Pulmonary hypertension	Severe cardiac failure
Severe restrictive lung disease	
Moderate to severe cardiac failure	
Severe valvular disease	
CKD stage 4-5	
Uncontrolled hypertension	
Previous early-onset pre-eclampsia or HELLP†	

Conception			
Safe to continue	Conditionally recommend to continue	Stop prior to conception	Unknown
Hydroxychloroquine Sulfasalazine Colchicine Azathioprine Certolizumab pegol Cyclosporine Tacrolimus	Prednisolone ^a Cyclosporine NSAIDs Infliximab Etanercept Adalimumab Golimumab Rituximab ^b Anakinra ^b Belimumab ^b Abatacept ^b Tocilizumab ^b Secukinumab ^b Ustekinumab ^b	Methotrexate Leflunomide Mycophenolate mofetil Cyclophosphamide Thalidomide	Tofacitinib Apremilast Baricitinib
Pregnancy			
Safe to continue	Conditionally recommend to continue	Stop prior to conception	Unknown
Hydroxychloroquine Sulfasalazine Colchicine Azathioprine Certolizumab pegol Cyclosporine Tacrolimus	Prednisolone ^a Cyclosporine NSAIDs ^c Infliximab ^d Etanercept ^d Adalimumab ^d Golimumab ^d Cyclophosphamide ^e Rituximab ^f	Methotrexate Leflunomide Mycophenolate mofetil Thalidomide Anakinra ^g Belimumab ^g Abatacept ^g Tocilizumab ^g Secukinumab ^g Ustekinumab ^g	Tofacitinib Apremilast Baricitinib

Lactation			
Hydroxychloroquine Sulfasalazine Colchicine Certolizumab pegol Infliximab Etanercept Adalimumab Golimumab Rituximab	Azathioprine ^h Prednisolone ^l Cyclosporine ^h Tacrolimus ^h NSAIDs ^l Anakinra ^k Belimumab ^k Abatacept ^k Tocilizumab ^k Secukinumab ^k Ustekinumab ^k	Methotrexate ^l Leflunomide Mycophenolate mofetil Cyclophosphamide Thalidomide	Tofacitinib ^m Apremilast ^m Baricitinib ^m

Pregnancy in Women Receiving Maintenance Dialysis

Cristina Popa,* Priyadarshini John,* Prasoon Verma, Sehrish Ali, and Silvi Shah



Women with kidney failure experience pathophysiological changes that frequently result in disruption of the hypothalamic-pituitary-ovarian axis. Because of these hormonal disturbances, women with kidney disease often experience oligomenorrhea, amenorrhea, sexual dysfunction, and infertility. Preconception counseling, partnered with the early identification and optimal management of risk factors, such as hypertension and discontinuation of teratogenic medications, should be pursued for females contemplating conception. Pregnancy in women receiving maintenance dialysis is associated with a high risk of adverse maternal and fetal outcomes and should be managed by a multidisciplinary team of providers. In this review article, we discuss pregnancy incidence, pregnancy outcomes, and management of pregnancy among women receiving maintenance dialysis.

Complete author and article information provided before references.

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In 1947, the first case report of peritoneal dialysis in a patient with eclampsia was published by Joan Marsden.¹ This marked the beginning of a new era in the management of pregnancy in women with kidney disease. However, nearly 30 years later, in 1975, *The Lancet* still noted that the children of women with kidney disease used to be born dangerously or not at all—not at all if their doctors had their way, highlighting the struggles of women with kidney disease and the approach of the medical community to pregnancy in this population.² Today, outcomes among pregnant women with kidney failure have improved through a

kidney transplantation, suggesting that the underlying cause of the hormonal imbalances with kidney failure is related to the dysfunction of the kidneys rather than permanent damage to the hypothalamic-pituitary-ovarian axis.^{5,6}

There is a high prevalence of menstrual abnormalities in women on maintenance dialysis, specifically irregular menses (47%) and amenorrhea (41%).⁷ Lin et al⁶ performed a cross-sectional study that showed a high prevalence of menstrual disturbances by kidney replacement therapy: nocturnal hemodialysis (55%), continuous ambulatory peritoneal dialysis (72.1%), and hemodialysis

Fertility and Kidney Failure

- Women with kidney failure experience disruption of the hypothalamic-gonadal axis that leads to irregularity in the menstrual cycle, anovulation, decreased libido, and impaired fertility.
- Women on maintenance dialysis, especially with amenorrhea, have **high serum prolactin** because of impaired kidney clearance, **increased** luteinizing hormone and follicular stimulating hormone, and **decreased** estradiol and progesterone concentration.
- The persistently elevated gonadotropins because of loss of negative feedback on hypothalamic and pituitary centers and absence of luteinizing hormone surge leads to anovulation

Menstrual abnormalities:

There is a high prevalence of menstrual abnormalities in women on maintenance dialysis

- Specifically irregular menses (47%)
- Amenorrhea (41%).

Cross-sectional study that showed a high prevalence of menstrual disturbances by kidney replacement therapy:

- Nocturnal hemodialysis (55%)
- Continuous ambulatory peritoneal dialysis (72.1%)
- Hemodialysis (76.1%)

sexual dysfunction

- The prevalence of sexual dysfunction is high among women on maintenance dialysis and is caused by hormonal derangements in addition to psychosocial factors, such as anxiety, depression, and poor social and body image.
- Hormonal changes may lead to dry skin, increased wrinkles, urinary incontinence, hot flashes, vaginal dryness, and atrophy, which may be associated with sexual dysfunction.
- In the population treated with dialysis, negative body image from feeling bloated, having edema, dialysis fistulas, catheters, or equipment in the bedroom has been listed as a factor contributing to decreased sexual satisfaction and desire
- **Women** are less content with their physical appearance than men and have a more negative impression of their bodies, particularly regarding sexual activity

Incidence of Pregnancy Among Women Receiving Maintenance Dialysis

- The pregnancy rate among women aged 15-44 years receiving dialysis is w18 per 1,000 person-years in the United States, with the highest rate being observed in women aged 20-24 at w41 pregnancies per 1,000 person years.
- Women treated with peritoneal dialysis have a 53% **lower** likelihood of pregnancy than those treated with hemodialysis

Pregnancy rate:

Review

Kidney Medicine

Pregnancy in Women Receiving Maintenance Dialysis

Cristina Popa,* Priyadarshini John,* Prasoon Verma, Sehrish Ali, and Silvi Shah



The reasons for the lower rates of conception among women receiving peritoneal dialysis remain :

- Unclear
- Although it is hypothesized that **hypertonic dextrose solutions**
- The presence of fluid in the peritoneal cavity may interfere with ovum transit to the uterus.
- Women with kidney failure because of malignancy, glomerulonephritis, hypertension, and secondary glomerulonephritis/vasculitis have **a higher pregnancy** rate than women with kidney failure because of diabetes.

Pregnancy Outcomes Receiving Maintenance Dialysis

- Pregnancy among women receiving maintenance dialysis is associated with a higher risk of adverse outcomes.
- The rate of premature birth is much higher among pregnant women receiving hemodialysis when compared with the general population, with a 2016 meta-analysis by noting that 88% of births were preterm among patients treated with dialysis.
- Another the Australia and New Zealand Dialysis and Transplant Registry study also reported that, premature births among pregnant women receiving hemodialysis were quite high

Poorer peripartum outcomes:

Pregnant women receiving hemodialysis have

- A higher rate of cesarean section, >60%
- A higher rate of blood transfusions
- Longer hospital stays with more than half of the patients staying >6 days in the hospital
- A higher risk of sepsis, which occurs in 6% of deliveries

Continue....

Review

Kidney Medicine

Pregnancy in Women Receiving Maintenance Dialysis

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- The rate of live births is lower
- The perinatal mortality is higher among women undergoing dialysis.
- Using United Renal Data System Data, Shah et al 13 reported that
- live births occurred in 27% of pregnancies
- 3% of pregnancies resulted in stillbirth
- 29% resulted in spontaneous abortion
- 8% of pregnancies had therapeutic abortion
- 3% had ectopic/trophoblastic pregnancies

Management of Pregnancies on Maintenance Dialysis

- Managing a pregnant patient receiving maintenance dialysis can be challenging because of the higher risk for maternal and fetal complications,
 - Preeclampsia
 - Fetal growth restriction
 - Preterm delivery
 - Stillbirths
 - Neonatal deaths



A multidisciplinary team consisting of the obstetrician, the nephrologist, a dietitian, and a maternal-fetal medicine physician should be engaged before, during, and after pregnancy

Preconception Counseling and Contraception

- Preconception counseling should include **a discussion** about the risks and benefits of pregnancy for all women of childbearing age who are receiving maintenance dialysis.
- **Kidney transplantation** should be encouraged, as reproductive function improves after kidney transplantation, and pregnancy post kidney transplantation is associated with fewer maternal and fetal complications.
- All women of childbearing age who are sexually active and do not wish to become pregnant should **be advised to be on contraception**.

Pregnancy in Women Receiving Maintenance Dialysis

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Contraceptive use:

- Irregular menstrual cycles in this population make it difficult to rely solely on natural family planning methods to avoid conception.
- Although this discussion should be held by both gynecologists and nephrologists, it is often **overlooked** by nephrologists.
- A survey performed in the United States by Sachdeva et al²¹ showed that only **46% of nephrologists** or their staff members counseled childbearing women about contraception.
- There is limited education and training on how to discuss and address reproductive health for women with kidney failure, which may result in a lack of confidence.
- Consequently, contraceptive use in female patients on maintenance dialysis is low

	Contraception method	Pros	Cons	Particularities in Kidney Failure
0.15-0.5	Sterilization 	- Either female or male - Very low failure rate	- Permanent - For women who do not want more children and have a scheduled cesarean delivery	Higher risk of hemorrhage and infection compared with general population
<0.1	Intrauterine device 	No need to remember taking medication	Complications include uterus perforation, though rare	Not recommended in patients with urinary malformations, pyelonephritis, and if peritoneal dialysis
0.2	Progesterone injection 	Only needed once every 3 months	May decrease bone mineral density	- Spotting may be more frequent because of anticoagulation during hemodialysis - World Health Organization does not recommend to be used by patients with antiphospholipid antibodies
0.3	Estrogen/progesterone combination 	Multiple options to fit patients preference	Increased risk of venous thromboembolism	- Contraindicated with antiphospholipid syndrome, kidney transplant with acute/chronic rejection, uncontrolled hypertension, diabetic nephropathy, significant cardiovascular risk 4th generation progestin may increase potassium because of their anti-mineralocorticoid effect
0.3	Progesterone only pill 	No increased risk of venous thromboembolism	- Requires strict adherence - To be administered within three hours from schedule daily time	World Health Organization does not recommend to be used by patients with lupus and antiphospholipid antibodies
Male condom 2 Female condom 5	Barrier methods 	Male condom is the only option to decrease the risk of sexually transmitted diseases	Should not be used alone, only together with other contraceptive method	

Oral contraceptive agents

- Oral contraceptive agents containing estrogen/progestin are commonly recommended to women of childbearing age as an effective birth control method and are associated with benefits, such as protection against ovarian cancer
- endometrial cancer On the contrary, combined hormonal contraceptives are associated with an increased risk of hypertension, cervical cancer, breast cancer, and ischemic stroke.





Should be used with caution:

- Combined hormonal contraceptives, containing both estrogen and progesterone, should be used with caution in :
- Patients receiving dialysis with uncontrolled hypertension
- Systemic lupus with positive antiphospholipid antibodies
- Because estrogen-containing contraceptives are associated with increased cardiovascular and thrombotic risks.

Progestin-only contraceptives

- May be used as an alternative as they have not been linked with worsening hypertension or ovarian, endometrial, and colorectal cancers.
- In comparison to combined hormonal contraceptives, progestin-only pills have a **lower** Contraception options for women receiving maintenance dialysis.

Continue.....

- The fourth-generation oral progestin, drospirenone, may theoretically increase potassium levels because of its anti-mineralocorticoid activity
- A meta-analysis of studies of women without kidney failure showed that the thrombotic risk was higher in women using progestin-only **injections** than non-users
- while progestin only pills or intrauterine devices did not increase this risk.
- In the general population, long-term use of progestin-only injection, depot medroxyprogesterone acetate, has been associated **with bone** mass loss and osteoporosis.

Other devices

- Intrauterine devices remain the **preferred method of contraception** because of low failure rates and are not associated with an increased risk of hypertension, thrombotic events, or cardiovascular events.
- Barrier methods, which include condoms, diaphragms, cervical caps, and sponges, are nonhormonal contraceptives and not recommended for use because of their high failure rate.
- Sterilization, which includes female tubal ligation and male vasectomy, is the only permanent contraceptive method available



Prenatal Care:

- Preconception counseling on the higher risk of adverse maternal and fetal outcomes with pregnancy among women receiving maintenance dialysis is imperative.
 - In women with autoimmune diseases, such as lupus nephritis, it is recommended to postpone conception until the disease is inactive for **at least 6 months** before conception to reduce the risks of adverse maternal and fetal outcomes.
-
- Low-dose aspirin should be started by the end of the first trimester for all pregnant women receiving maintenance dialysis to reduce the risk of preeclampsia.
 - The recommended blood pressure (BP) goal during pregnancy is < 140/90 mm Hg.
 - Folic acid is removed with hemodialysis, and the dose should be increased to 5 mg following conception



Anticoagulation in Pregnancy



- Anticoagulation during pregnancy is recommended in patients with kidney failure with risk factors for venous thromboembolism, including
 - Nephrotic range proteinuria
 - Hypoalbuminemia with serum albumin < 2 mg/dL
 - Positive antiphospholipid syndrome
 - Previous history of thrombosis
- Anticoagulation can be considered for patients with additional risk factors such as immobility and obesity and patients with higher risks of thrombosis such as membranous nephropathy and vasculitis.
- Current guidelines recommend unfractionated heparin or low molecular weight heparin for anticoagulation during pregnancy and 6 weeks postpartum



Medication Optimization

- Nephrologists should thoroughly review medications during preconception counseling.
- Teratogenic medications should be discontinued at least **6 weeks** before planned conception.
- If an unexpected pregnancy occurs, these medications should be discontinued immediately after the diagnosis is made.
- Women who have received a cumulative dose of more than 10 gm of cyclophosphamide in the past should be assessed early for infertility, and, if assisted reproduction techniques are sought, single embryo transfer should be pursued

	SAFE	UNSAFE
 Antihypertensives	- Labetalol - Dihydropyridine calcium channel blockers (nifedipine, amlodipine) - Methyldopa - Hydralazine	- Renin-angiotensin system inhibitors - Atenolol - Spirolactone
Immunosuppression	- Glucocorticoids - Calcineurin inhibitors - Hydroxychloroquine - Azathioprine	- Mycophenolate - mTOR Inhibitors (sirolimus) - Cyclophosphamide
Anemia	- Erythropoietin - Iron	- Hypoxia-inducible factor prolyl hydroxylase inhibitors - Roxadustat, contraindicated during third trimester, caution during first two trimesters
Mineral Bone Disease	- Calcium-based phosphate binders - Calcitriol	- Little data on use of non calcium based phosphate binders (sevelamer, lanthanum) - Cinacalcet
Anticoagulants	- Heparin - Low molecular weight heparins	- Warfarin - Direct anticoagulants
Other medications	- Double dose of water-soluble vitamins - Folic acid	- Non-steroidal anti-inflammatory drugs - Statins

Anemia

- Anemia may worsen during pregnancy because
 - of volume expansion
 - increased demands of the growing fetus.
- Increased doses of parenteral iron (oral or intravenous) and erythropoietin-stimulating agents may be needed during pregnancy to maintain a hemoglobin level of **10-11 g/L**.
- For hyperphosphatemia during pregnancy, **calcium-based binders** and **vitamin D analogs** are preferred over non-calcium-based phosphate binders or calcimimetics because of limited data on the latter agents with pregnancy

Hypertension Management

- Hypertension during pregnancy is associated with many adverse maternal and fetal outcomes, such as maternal cardiovascular complications, fetal morbidity, intrauterine growth restriction, and premature delivery.

The American College of Obstetricians and Gynecologists Task Force has classified hypertension in pregnancy into 4 categories:

- Chronic hypertension
- Gestational hypertension
- Preeclampsia
- Preeclampsia superimposed on chronic hypertension.
- Chronic hypertension is a pre-existing diagnosis of hypertension before 20 weeks of gestation or persistent hypertension > 12 weeks postpartum.

Continue.....

- Gestational hypertension is new-onset hypertension, defined as BP $\geq$ 140/90mm Hg after 20 weeks of gestation without any proteinuria or end-organ.
- Preeclampsia is defined as new-onset hypertension after 20 weeks of gestation with proteinuria ($\geq$ 300mg/d) or end-organ dysfunction in at least 1 organ.
- End-organ damage can include thrombocytopenia (platelet count $<$ 100,000/ μ L), kidney dysfunction (serum creatinine $>$ 1.1mg/dL or doubling of the serum creatinine concentration in the absence of other kidney disease), liver enzymes twice the upper limit of normal range, pulmonary edema, or new-onset cerebral or vision changes

Preeclampsia:

- Preeclampsia superimposed on chronic hypertension is new-onset proteinuria or end-organ dysfunction coupled with worsening hypertension after 20 weeks of gestation in women with chronic hypertension.
- In women treated with dialysis, it is challenging to diagnose preeclampsia especially among those with pre-existing hypertension because of limited utility of urine protein creatinine ratio with anuria.
- New onset of hypertension after 20 weeks or worsening of hypertension in women with pre-existing hypertension along with classical symptoms (headache, nausea, vomiting, epigastric pain, and visual disturbances) and laboratory abnormalities (hemolysis, thrombocytopenia, liver dysfunction, and high uric acid) of end-organ damage can be used to make a diagnosis of preeclampsia.

Continue.....

- A multicenter randomized clinical trial in the general population, the control of hypertension in pregnancy study, compared tight BP control (diastolic BP of 85mm Hg) to less tight BP control (diastolic BP>100mm Hg), and found that the tight BP group had less incidence of severe hypertension (BP>160/110mm Hg), but the risk of adverse pregnancy outcomes was **not significant**.
- Achieving a BP of<140/90mm Hg was associated with lower adverse pregnancy outcomes in comparison with the control group
- Based on these trials in the general population, we recommend to attain a **BP goal of<140/90mm Hg during pregnancy in women on maintenance dialysis**

Delivery:

- For patients with preeclampsia, delivery is recommended at 37 weeks or later if no severe features such as hemolysis, thrombocytopenia, or liver dysfunction are observed.
- Stabilization and delivery at or >34 weeks are recommended in those women with severe features or adverse maternal or fetal conditions, such as fetal growth restriction or fetal distress.
- If delivery is done before 34 weeks' gestation, corticosteroids should be administered to the mother for fetal lung maturity.
- Many patients with preeclampsia are treated with magnesium sulfate to minimize the risk of seizures.
- As magnesium is excreted by kidneys, a lower dose is recommended for women with kidney failure. Careful monitoring for clinical signs of magnesium toxicity and magnesium levels is needed

Fetal and Maternal Monitoring during Pregnancy

- Despite the best care offered to pregnant dialysis women, only 75%-80% of pregnancies reach the second trimester with surviving infants, out of which 82% are born premature.
- Fetal morbidity can be because of premature rupture of membranes, premature labor, and cervical incompetence.
- The incidence of cervical incompetence is high in women treated with dialysis, and screening is suggested between 18 and 20 weeks.
- Preeclampsia should be screened by monitoring BP and laboratory chemistries, including complete blood counts and liver function tests, twice a month. Minimizing fluctuations in BP during dialysis sessions prevents uteroplacental insufficiency.
- For a patient receiving dialysis, pregnancy is considered high risk, and fetal anomaly screening is recommended

Peritoneal Dialysis During Pregnancy

- Although pregnancy is rare in women who are receiving peritoneal dialysis because of the possible effects of hypertonic dialysate on the transit of the ovum to the uterus, women can continue pregnancy on peritoneal dialysis with modifications in peritoneal dialysis prescriptions.
- The advantages of peritoneal dialysis during pregnancy are controlled ultrafiltration, better hemodynamic stability, a lesser incidence of anemia, better control of BP, and avoidance of anticoagulation.
- As the gestational age increases, peritoneal dialysis becomes difficult for many patients.
- With the increasing size of the uterus, effective peritoneal exchanges may not take place because of a reduction in effective peritoneal surface area, even though the peritoneal membrane continues to maintain the clearance and ultrafiltration capability during pregnancy.
- Thus, the prescription may need to be adjusted during pregnancy to reduce the dwell volume and increase the number of exchanges.
- A successful pregnancy occurring during peritoneal dialysis may also depend on residual kidney function. Women with residual **urine output of >500mL** have been shown to have better fetal and maternal outcomes

peritoneal dialysis prescriptions

- Intensify the prescription by decreasing the dwell volume and increasing the frequency of exchanges.
- This may be facilitated using cyclers, particularly in the second trimester and beyond.
- Use both manual daytime exchanges and cycler-assisted overnight exchanges to facilitate adequate dialysis in the third trimester, a time during which further reduction in the dialysate volume is needed.
- Use tidal peritoneal dialysis, which leaves 15% of the dwell volume in situ while draining, to reduce drain pain and gastroesophageal reflux.
- Minimize the use of highly hypertonic peritoneal dialysate like that containing 4.25% dextrose.
- Adopt right or left lateral decubitus position during the draining phase.

Peritoneal Dialysis Prescription During Pregnancy



Intensify manual peritoneal dialysis with reduced dwell volume and multiple exchanges



Automated peritoneal dialysis with small volumes and augmented exchanges assisted with cyclor



Tidal peritoneal dialysis-15% infused volume is retained during drain phase



Caution with very high tonicity peritoneal dialysate



Lateral decubitus posture during draining phase

Continue.....

- Although it is not a regular practice to check the adequacy of peritoneal dialysis during pregnancy, a Kt/V between 2.2 and 2.4 is recommended, which usually requires a daily dialysate volume of about 20 liters.
- A suggested calorie intake of 25kcal/kg/d is recommended during pregnancy for those receiving peritoneal dialysis.

Complications associated with peritoneal dialysis

- Peritonitis
- Exit site infections
- Catheter displacement
- Hemoperitoneum
- Drain pain
- Gastroesophageal reflux
- In rare instances, postpartum peritonitis and traumatic uterine rupture from peritoneal catheter.
- Polyhydramnios (excess amniotic fluid), though rare among women receiving peritoneal dialysis, may occur if maternal urea levels are high enough to cause an osmotic diuresis in the fetus causing increased urine production by the fetus.
- Monitoring for electrolyte derangements such as hypokalemia and hypophosphatemia is essential to prevent arrhythmias and other fetal complications, and supplementation is warranted accordingly

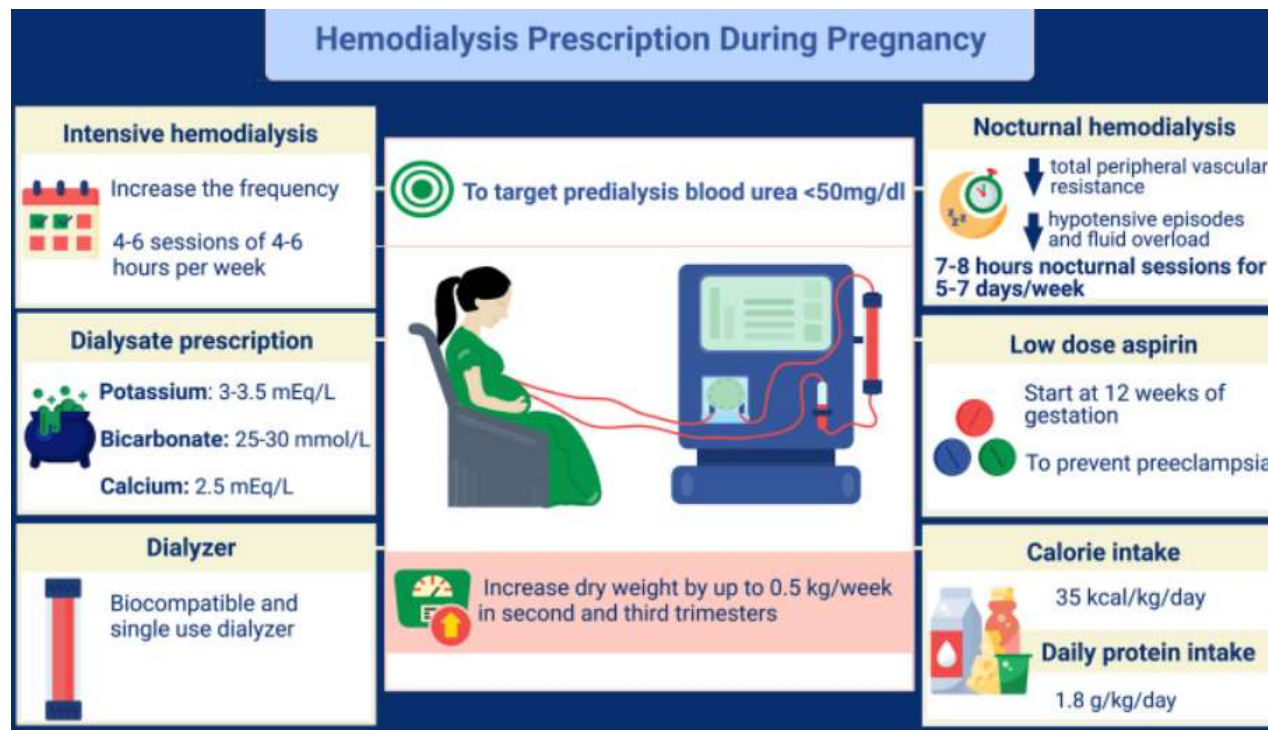
Hemodialysis During Pregnancy

- Intensive hemodialysis is recommended during pregnancy because it is associated with better fetal and maternal outcomes.
- Up to 36 hours of dialysis weekly is recommended for women, targeting predialysis serum **blood urea nitrogen** of $<50\text{mg/dL}$.
- In a series of 344 pregnancies, observed that infants born to women who had >20 hours/wk of dialysis had prolonged gestational age and a higher birth weight.
- Intensive hemodialysis is associated with improved pregnancy outcomes with a lower incidence of prematurity, a higher incidence of live birth rate, higher birth weight, and lower neonatal mortality rate

- To achieve a pre dialysis blood urea of less than 50mg/dL, 4-6 sessions of 4-6 hours of dialysis per week are usually needed.
- Frequent dialysis is aimed at maintaining adequate uteroplacental flow without compromising on net fluid removal.
- **Biocompatible and single-use dialyzers** are recommended to prevent fetal toxicity secondary to reuse agents such as formaldehyde and ethylene oxide.
- Respiratory alkalosis with compensated metabolic acidosis is usually seen during pregnancy. Hence, dialyzing a pregnant woman would mandate low bicarbonate dialysate to avoid alkalemia. Although the data are limited, it is recommended to use a dialysate bath with 25-30mmol/L bicarbonate during pregnancy.
- To minimize the risks of hypocalcemia, hypokalemia, and hypophosphatemia in the mother, it is recommended to use dialysate with a **calcium concentration of 2.5 mEq/L** and dialysate potassium between **3 and 3.5 mEq/L**.⁷
- **Periodic monitoring** of calcium, phosphorus, and other electrolytes is suggested for early identification and correction of electrolyte abnormalities

Ultrafiltration during dialysis:

- Ultrafiltration during dialysis in a pregnant woman can be challenging.
- Fetal weight gain after the first trimester is mostly constant at 0.3-0.5kg per week.
- Therefore, as long as the patient is euvolemic, the dry weight can be increased by 400 gm per week to account for the growing fetus weight of 500 gm per week.
- Slow continuous ultrafiltration can be considered for excessive weight gain or refractory fluid overload states during pregnancy.



Nocturnal hemodialysis

- Nocturnal hemodialysis in pregnant women is safe, and women who conceived while utilizing nocturnal hemodialysis as their kidney replacement therapy can continue with the modality.
- Women receiving nocturnal hemodialysis tend to have decreased total peripheral vascular resistance, which decreases the incidence of fluctuating BP or volume overload.
- Nocturnal hemodialysis prescriptions during pregnancy usually require 7-8 hour sessions, 5-7 days a week.
- Women performing nocturnal hemodialysis might require **phosphate supplementation** in the dialysate to avoid hypophosphatemia because of prolonged dialysis sessions

Conclusion

- This review presents the current best practices in evaluating and managing pregnant women on maintenance dialysis.
- Women with kidney failure undergoing dialysis must be counseled regarding the increased risk of maternal and fetal complications with pregnancy.
- A multidisciplinary team consisting of a nephrologist, maternal-fetal medicine specialist, and neonatologist should manage pregnancy in women receiving dialysis

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The most common ones:

- Among the GDs diagnosed by kidney biopsies in pregnancy or in the postpartum period, the most common ones:

- FSGS
- IgA nephropathy (IgAN)
- LN

Other GDs are rare, but most of them have been reported in pregnancy.

- Much more is known about the prevalence of GDs in pregnant women on renal replacement therapy:
- 35% to 56% of women on chronic dialysis or those having received a kidney transplant have a GD **as their primary** renal disease.

TOOLS FOR THE DIAGNOSIS AND MONITORING OF GDs IN PREGNANCY

- A decrease in kidney vascular resistance
- An increase in kidney blood flow
- Concomitant increase in glomerular filtration rate (38%–56% increase in creatinine clearance), by the first trimester of pregnancy.
- There is currently no widely accepted formula for the estimation of kidney function in pregnancy.
- Some authors consider urinary creatinine clearance as the gold standard—and adding 24-hour urine collection allows for a better assessment of proteinuria.
- Others recommend evaluating kidney function using serum creatinine concentration

Marker of renal function outcome.

- Staging of CKD in pregnant patients with a GD should be based on prepregnancy values, whenever possible.
- The absence of an early decrease in serum creatinine during pregnancy compared with prepregnancy concentrations has been proposed as a poor prognostic marker of renal function outcome.
- Glomerular hyperfiltration, however, has not been associated consistently with better pregnancy-related out-comes, at least during the early stages of CKD.
- Longitudinal kidney function (e.g., decrease of estimated glomerular filtration rate in midterm) in pregnancy may be as relevant as the baseline absolute values.

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- As with estimated glomerular filtration rate estimations, there is no consensus regarding the best method for assessing proteinuria in pregnancy.
- Use of the spot urinary protein-to-creatinine ratio (UPCR) is usually preferred to timed urine collections because of the possibility of underestimation, variability, and inconvenience, and the potential for treatment delay with the latter.
- The UPCR is practical for screening for hypertensive disorders of pregnancy, for which new onset of proteinuria (UPCR >30 mg/mmol) is still one discriminating parameter between preeclampsia and gestational hypertension.
- The recently proposed option of calculating the UPCR and/or urinary albumin-to-creatinine ratio from a 16- to a 24-hour urine collection may be utilized in pregnant patients with GDs.
- The approach balances the advantages of a 24-hour urine collection with the practical constraints of this test

RISK EVALUATION FOR PREGNANCY

Three major determinants of pregnancy-related outcomes are identified:

- kidney function impairment—the most extensively studied
- Probably the most important factor—proteinuria,
- Hypertension

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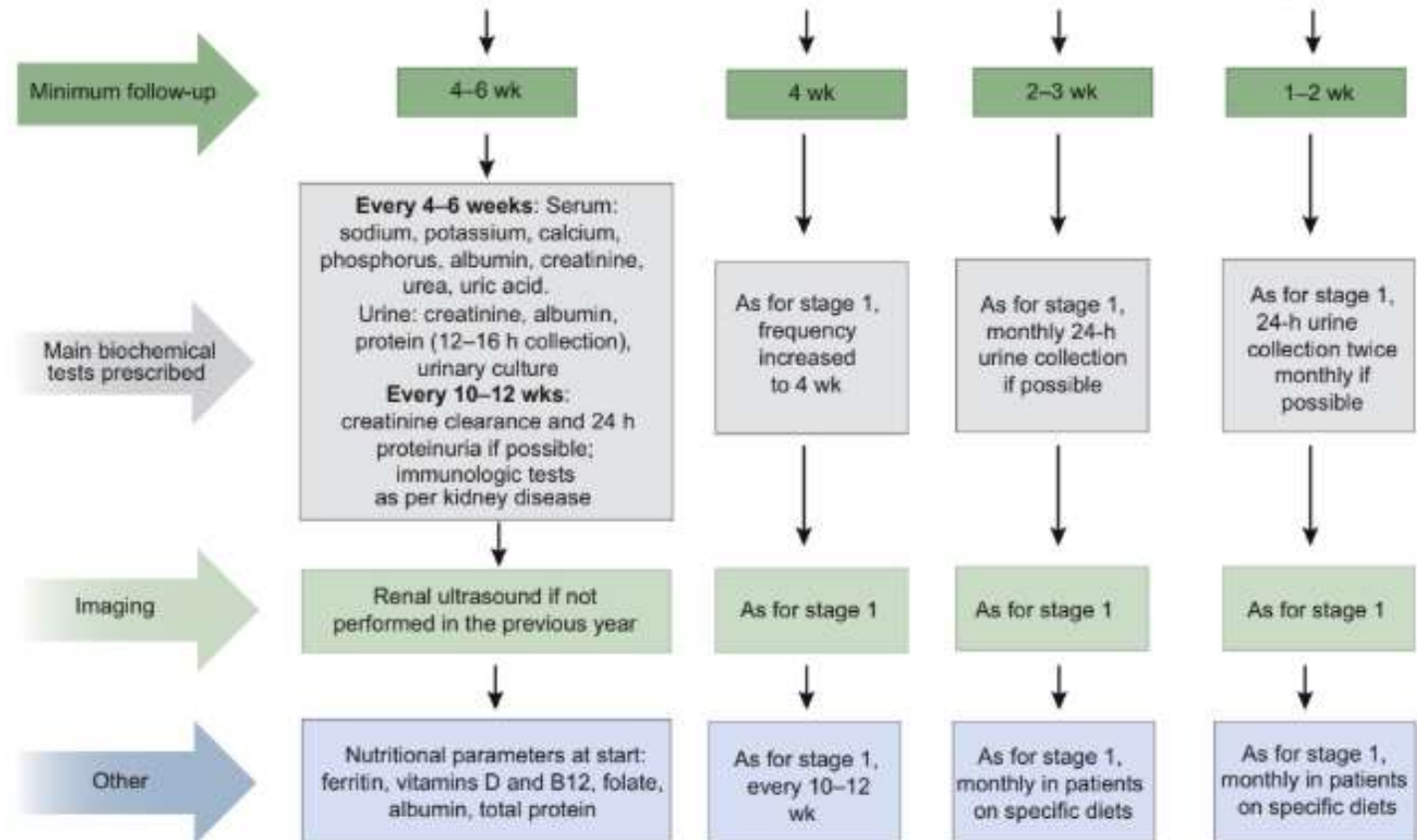
- As for maternofetal outcomes excluding kidney function, GDs generally seem to be associated with a higher risk of adverse pregnancy events compared with patients with other types of kidney diseases.
- This increased risk even applies to women with a GD and CKD stage 1, mild proteinuria (<1 g/24 h), or normal blood pressure (i.e., a GD in complete clinical remission).
- Pregnancy outcomes in these patients are similar to those of women with kidney transplantation

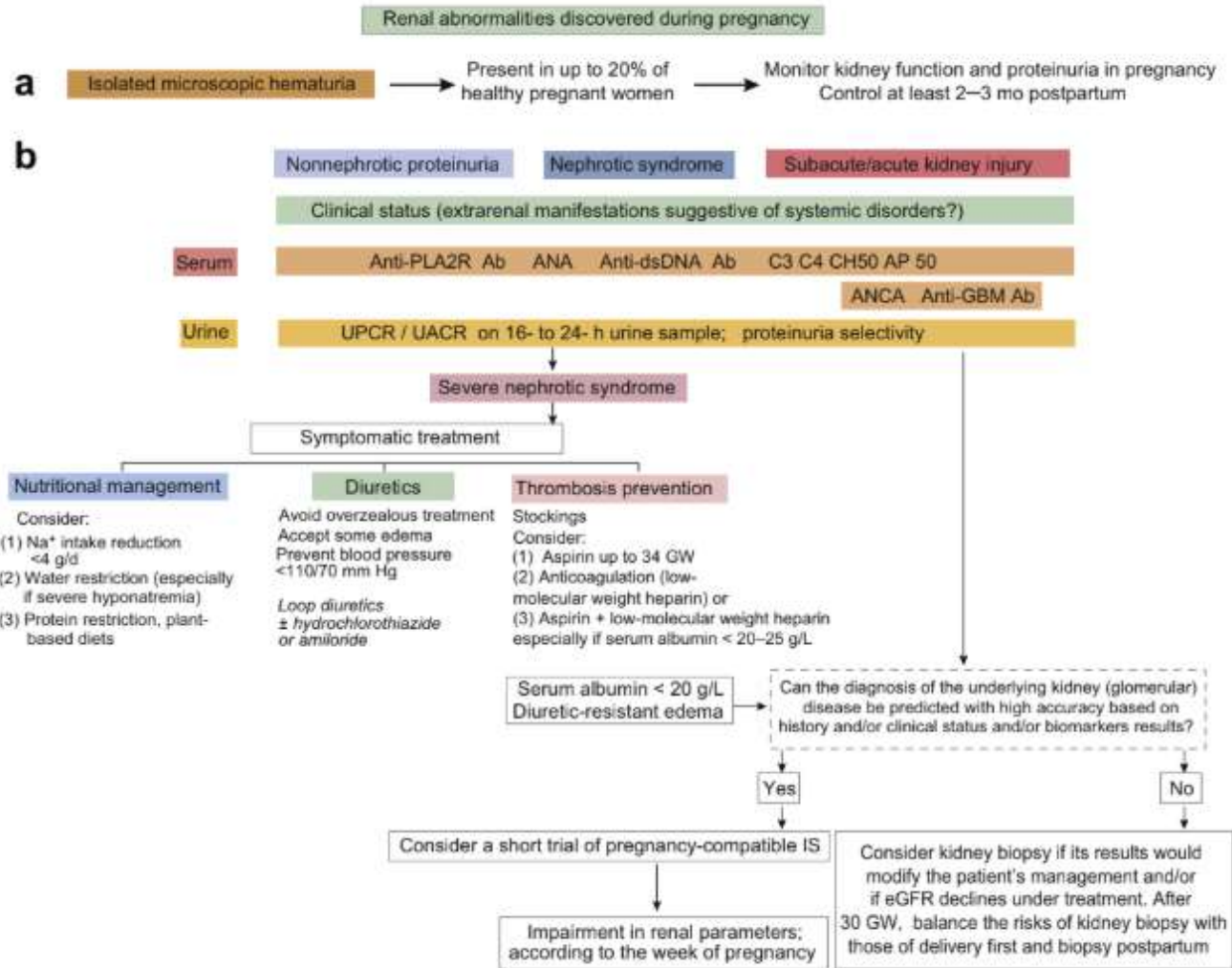
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- Conversely, with respect to kidney function, women with a GD and normal kidney function before pregnancy do not have a clearly increased risk of kidney function impairment during or after pregnancy, even in the long-term, compared with nonpregnant women with a GD.
- This finding has been documented particularly in women with IgAN and LN

How should women with GD and CKD starting a pregnancy be monitored?

**Glomerular diseases:
for tests and
follow-up during
pregnancy**





Obstetrical considerations

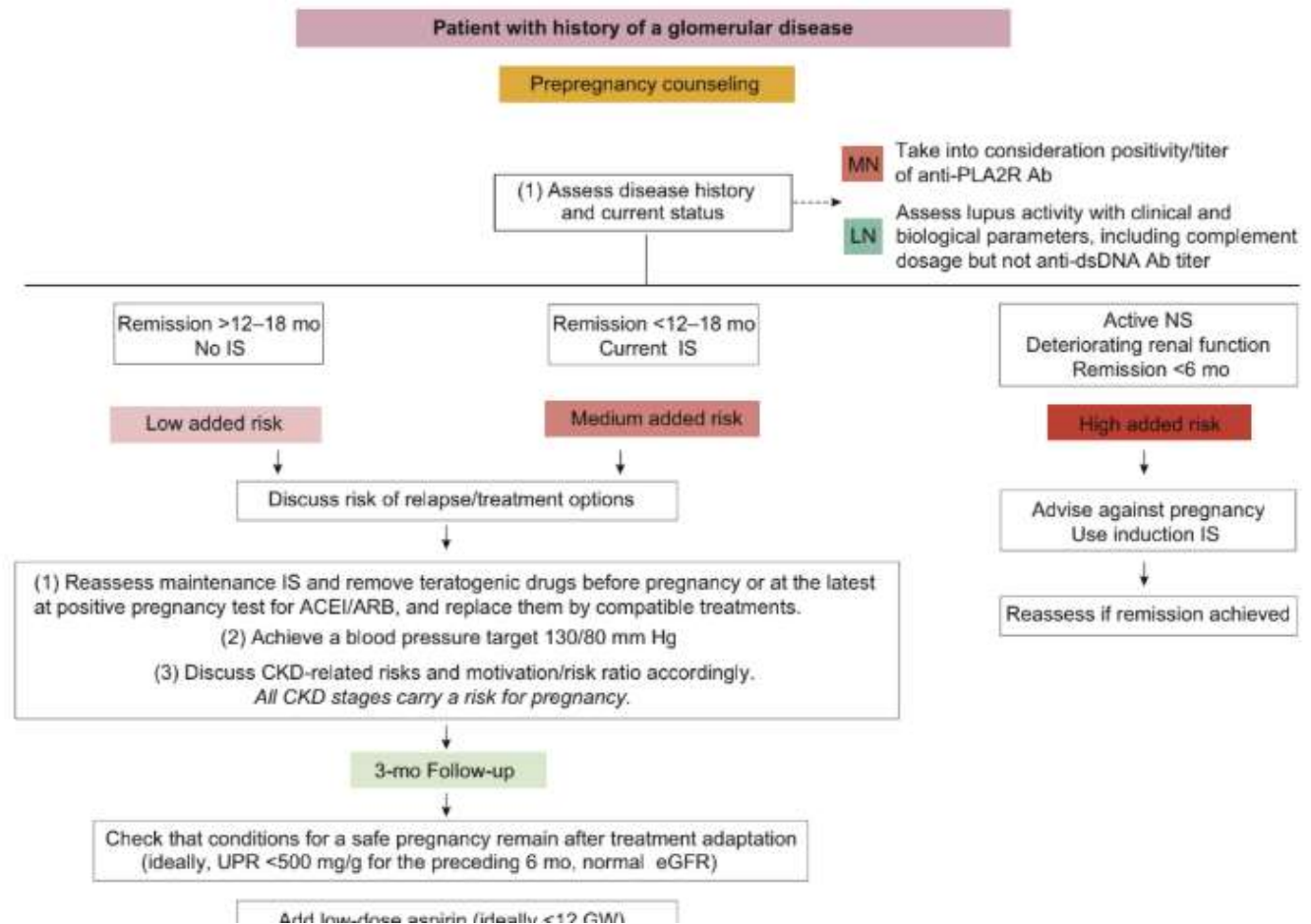
- The main obstetric risks are not specific to GD, as they include preeclampsia, preterm delivery, and intrauterine growth restriction.
- The risk of intrauterine death is also increased, particularly in women with lupus nephritis, diabetic nephropathy, and other systemic immunologic diseases.
- The severity of preeclampsia is variable; although it may be particularly severe, requiring early therapeutic termination of pregnancy for maternal
- Changes in proteinuria and blood pressure in patients with GD are not necessarily linked to preeclampsia, and may reveal flares of the underlying disease or, as for proteinuria, may be indicative of hyperfiltration stress.
- The differential diagnosis may be difficult
- The risks for offspring are mainly linked to preterm delivery, which does not only occur in the context of preeclampsia.
- The risk of intrauterine growth restriction is also increased, particularly in women with hypertension.

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- Ultrasound screening for fetal growth retardation should be performed monthly, as for other pregnancies at risk for fetal growth restriction.
- The frequency of using Doppler ultrasounds should be tailored on the basis of the presence and severity of abnormalities.
- Obtaining available biomarkers to determine the angiogenic-antiangiogenic balance may assist in clinical management;
- to prevent or attenuate severe complications in these high-risk pregnancies.
- (vii) The use of low-dose aspirin prophylaxis is currently a standard of care in all pregnancies at risk for PE, including those in women with GD.⁷⁰
- Early start (<12 gestational weeks) is indicated to warrant efficacy; treatment is stopped between 34 and 36 gestational weeks, or in the presence of risk conditions for imminent delivery.
- Vitamin D deficiency should be corrected

Practical recommendations for the counseling of women with GD who plan or start a pregnancy

- Take into account the woman's wish during the counseling, in a shared decision approach.
- Integrate psychological aspects of pregnancy in women with GD, which are at least as important as medical aspects.
- Individualize the assessment of pregnancy risks to the patient's clinical and biological features.
- Give as much as possible an objective assessment of the risk of adverse pregnancy outcomes and progression of CKD.
- Highlight the areas of uncertainty, the individual response, as well as the lack of available precise data stratified per kidney function, degree of proteinuria and hypertension, and type of GD.
- In women with eGFR <30 ml/min at the start of pregnancy, discuss the issue of potential dialysis need, during pregnancy or shortly after delivery.
- Explain the need to adapt treatment before/at the start of pregnancy and the therapeutic options in case of potential relapse/exacerbation of GD during pregnancy.
- Discuss the potential need for induced/premature delivery and prematurity-related complications for the newborn.



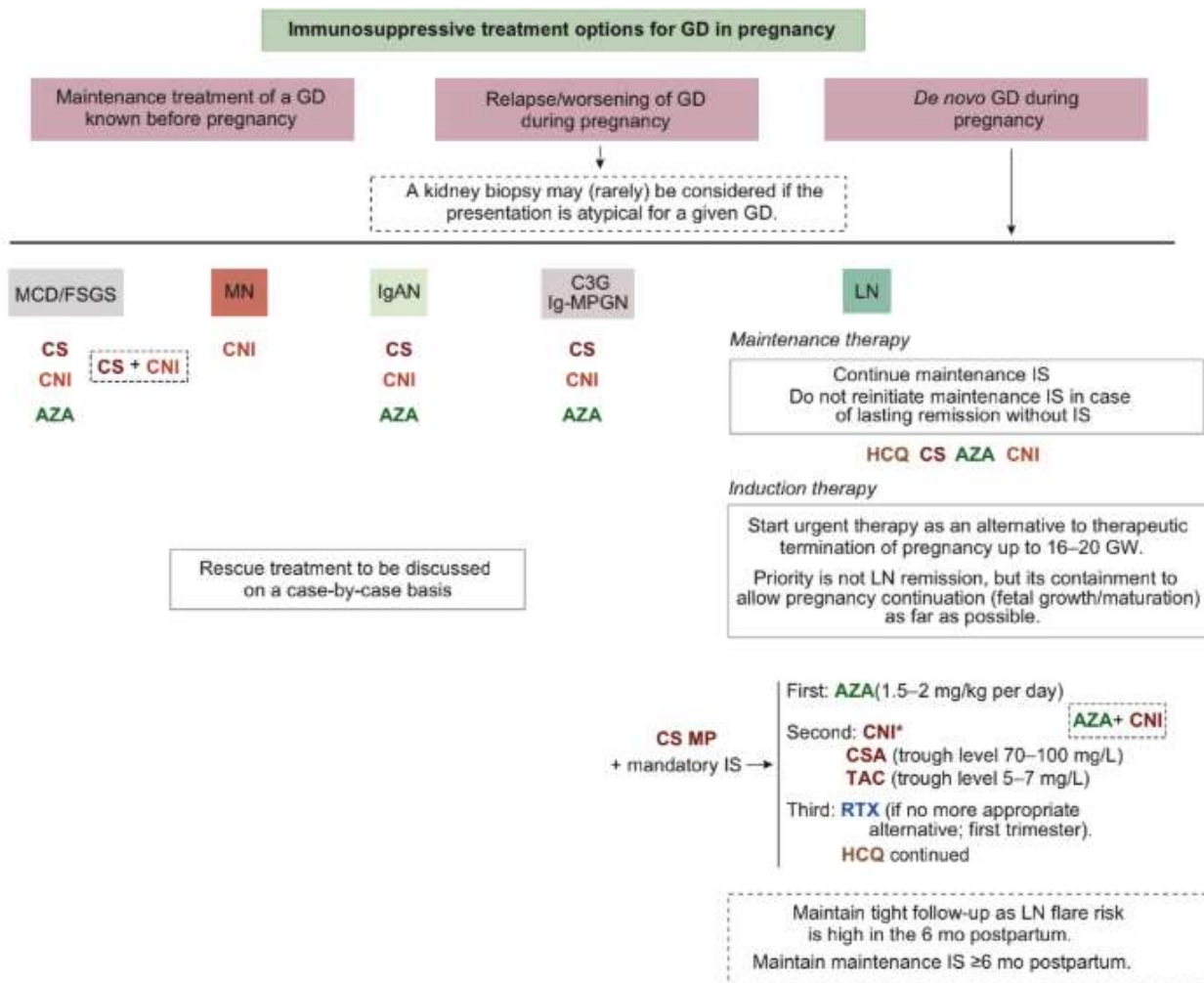


Table 5 | Antihypertensive drugs for emergency and nonemergency hypertensive disorders of pregnancy in women with GD

Setting	Drug	Route	Dose	Contraindications	Adverse effects
Emergency	Labetalol	I.v.	10–20 mg initially, then 20–80 mg every 10–30 min to a maximum cumulative dose of 300 mg; infusion: 1–2 mg/min	Second- or third-degree AVB Systolic heart failure Asthma bradycardia	Bronchoconstriction Fetal bradycardia
	Urapidil	I.v.	12.5–25 mg as bolus injection; 5–40 mg/h as continuous infusion		Hypotension Reflex tachycardia
	Hydralazine	I.v.	5 mg, then 5–10 mg every 20–40 min		Hypotension Reflex tachycardia Headaches
No emergency	Labetalol	Oral	100 mg bid to 800 mg tid	Second- or third-degree AVB Systolic heart failure Asthma Bradycardia	Bronchoconstriction Fetal bradycardia
	Nifedipine	Oral	20–30 mg bid		Reflex tachycardia Headaches
	α -Methyldopa	Oral	250 mg bid to 1000 mg tid; titrate every 48 h		Orthostatic hypotension Sedation

AVB, atrioventricular block; bid, 2 times a day; GD, glomerular disease; tid, 3 times a day.



