Glomerular Disease and Pregnancy

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Nephrologists are routinely involved in the care of pregnant women with glomerulonephritis. Prepregnancy counseling is vital to inform women of the potential risks of pregnancy and to reduce those risks by optimizing clinical status and medications. In general, for all glomerulonephritides, the best pregnancy outcomes are achieved when the disease is in remission and the woman has preserved renal function with no proteinuria or hypertension. Each glomerulonephritis has specific considerations, for example in lupus nephritis, mycophenolate is teratogenic and must be stopped at least 6 weeks before conception, hydroxychloroquine is recommended for all pregnant women, and flares are frequently encountered and must be treated appropriately. De novo glomerulonephritis should be considered when significant proteinuria is found early in pregnancy or an acute kidney injury with active urine is encountered. Biopsy can be safely undertaken in the first trimester. Treatment is often with corticosteroids, azathioprine, and/or tacrolimus. Rituximab is increasingly used for severe disease. Women with glomerulonephritis should ideally be managed in a joint renal-obstetric clinic. This review details the approach to the care of women with glomerulonephritis from prepregnancy counseling, through antenatal care and delivery, to the postpartum period. Special attention is given to medications and treatment of glomerulonephritis in pregnancy.

Key Words: Glomerulonephritis, Pregnancy, Lupus nephritis, Glomerular disease, Preconception counseling, Vasculitis

Historically, women with glomerulonephritis (with the notable exception of lupus nephritis) rarely got pregnant – mostly at the behest of their doctors. Improvements in both medical care and fertility technology mean pregnancy is a feasible option for more and more women, and as a result, nephrologists need to be proficient in issues such as fertility, teratogenicity, and pregnancy.

Choice of initial and maintenance immunosuppressive therapies, use of adjunctive therapies such as antihypertensives, use of contraceptives, and even timing of biopsy will all need to be given special consideration in women of child-bearing age. Pregnancies should be planned in advance with therapies modified to facilitate successful conception, pregnancy, and delivery. Ideally, all women should receive prepregnancy counseling with a specialist obstetric nephrologist or obstetric physician.[1] However, we recognize this service is not available everywhere and often it will be their usual nephrologist providing this service.[1] The aim of this review is to discuss the management of women with glomerulonephritis before pregnancy, antenatally and postnatally.

MANAGEMENT OF WOMEN OF CHILD-BEARING AGE WITH A GLOMERULAR DISEASE

The best maternal and fetal outcomes in women with a history of glomerulonephritis are in those with preserved renal function, minimal proteinuria, and no hypertension. Therefore, the main priorities are early diagnosis and effective treatment. The potential impact of the treatment on future fertility should be discussed with all women of child-bearing age. Where treatments are equally effective (eg, mycophenolate mofetil vs cyclophosphamide for induction treatment of lupus nephritis),[2] the fertility-preserving treatment should be considered. If a fertility-affecting treatment must be used, steps to protect fertility should be discussed (eg, low-dose cyclophosphamide, gonadotrophin antagonists,[3] involvement of fertility specialists and/or freezing embryos).[4] Women receiving treatments where pregnancy is contraindicated (eg, cyclophosphamide, mycophenolate, methotrexate) must be informed of the risk and be advised to use effective contraception. Long-acting, reversible contraception is ideal (eg, Mirena coil or Nexplanon) as they are safe and extremely effective. The progesterone-only pill is also an acceptable choice.[1] Estrogen-containing contraceptives are associated with increased risks of venous thromboembolism, arterial disease, hypertension, and breast and cervical cancer, which mean they are an inappropriate choice of contraception for many women with glomerular disease. There are also concerns they may be associated with disease flares in lupus nephritis.[5] Condoms, with typical use, have a 19% failure rate per year and cannot be recommended as acceptable contraception.[1]

Prepregnancy Counseling

Prepregnancy counseling offers a number of unique opportunities including reviewing the diagnosis and activity, medications, and potential impacts of pregnancy on the disease and the disease on pregnancy. This allows women to make an informed choice before pursuing pregnancy.[5] Where a prepregnancy consultation has not taken place many of these discussions around risks, impact on disease and likely pregnancy course will take place at the first antenatal appointment when it might be too late to optimize disease status, stop teratogenic medications, or prevent an ill-timed or unintended pregnancy.

Reviewing the patient's diagnosis and disease activity is vital for accurate and informed prepregnancy counseling. For all glomerulonephritides, pregnancy outcomes

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depend on disease activity before pregnancy, presence and degree of proteinuria, presence of hypertension, and degree of renal function.[6] To ensure the best maternal and fetal outcomes, any induction treatment should be completed and the patient be stable on pregnancy-safe maintenance immunosuppression or off treatment for at least 6 months before conception.[7] Pregnancy-safe medications should not be reduced or withdrawn immediately before or after conception as the overall aim is to maintain remission. Women with active disease should postpone pregnancy until their disease is quiescent. Where disease is unlikely to be controlled, a full discussion about the risks of pregnancy should be undertaken. Occasionally, a biopsy is undertaken at this stage to facilitate informed decision-making.[1] Women should be informed; they are likely to have a more medicalized pregnancy and delivery. Usually, they need obstetrician-led care (as opposed to midwife led), extra appointments, and scans during pregnancy and may need to deliver in a hospital setting.

Women (and doctors) often worry about medications and pregnancy. As well as reviewing and optimizing the patient's medications, prepregnancy counseling is the ideal time to reassure women as to which of their medications are safe in pregnancy and breastfeeding and the risks to themselves and to their pregnancy if stopped. In the authors' experience, acknowledging and discussing womens' anxieties about medications in pregnancy results in less fear and less inappropriate medication cessation during pregnancy. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers are commonly used to as renal protective agents in glomerulonephritis – however, second/third trimester exposure is associated with what can be a lethal embryopathy. ACE inhibitors can be continued until women fall pregnant and stopped once the pregnancy is confirmed and no later than 6 weeks gestation. Women with irregular menstrual periods need to perform regular pregnancy tests to ensure early pregnancy diagnosis.[8] Angiotensin receptor blockers should be stopped before conception. Occasionally, ACE inhibitors are stopped in anticipation of pregnancy to allow an assessment of baseline proteinuria. This can be advantageous later in pregnancy if the cause of increasing proteinuria is unknown and preeclampsia is being considered. Azathioprine,[9] tacrolimus,[10] cyclosporine,[11] and hydroxychloroquine[7] are all considered safe in pregnancy and breastfeeding. Rituximab[12] and steroids[13] can be given after consideration of the risks and benefits (discussed in the following). The risk of preeclampsia should be assessed, and where appropriate, a plan should be made to start low-dose aspirin (75-150 mg) in pregnancy.[14,15] Women with CKD, hypertension, and autoimmune diseases such as systemic lupus erythematosus (SLE) or antiphospholipid syndrome should all receive aspirin prophylaxis.[15] The authors would recommend prophylaxis to all women with glomerulonephritis with the exception of childhood nephrotic syndrome that has been in remission for many years. Women with significant proteinuria(>250 mg/mmol), hypoalbuminemia (<20-25 g/L),[16] or increased thrombotic risk[17] (eg, prior venous thromboembolism, venous thromboembolism in first degree relative, obesity, age >35 years) will need prophylactic low-molecular-weight heparin during pregnancy. Both low-dose aspirin and low-molecular-weight heparin are safe in pregnancy.[18] Many women with glomerulonephritis will require management of hypertension before and during pregnancy (whether preexisting, pregnancy-induced hypertension or preeclampsia). A blood pressure of 135/85 mmHg is targeted.[15,18] Labetalol and nifedipine are commonly used antihypertensives in pregnancy, either is an appropriate first choice.[19] Prepregnancy counseling is also an ideal time to discuss other general issues, for example if the patient is not planning pregnancy (yet or ever), they should be using long-acting, reversible contraception. They should also take folic acid 4 mg for 3 months before conception.[20]

CLINICAL SUMMARY

- Prepregnancy counseling is important for all women with glomerulonephritis who are considering pregnancy.
- It is vital that, where possible, any glomerulonephritis is in remission before pregnancy.
- Mycophenolate is teratogenic. Azathioprine, calcineurin inhibitors, and steroids are all safe in pregnancy.
- Women with glomerulonephritis should ideally be managed in a joint renal-obstetric clinic.

Prepregnancy counseling should also address disease-specific considerations for the individual glomerular disease; the impact of the glomerulonephritis on pregnancy, the impact of pregnancy on their glomerulonephritis, medications, and other special considerations – refer to disease-specific sections under antenatal care in the following.

Antenatal Care

Where possible, women with glomerulonephritis should attend a combined renal-obstetric clinic antenatally. They need regular blood pressure, urine protein:creatinine ratios (24-hour urine protein collections are not required), and blood tests (minimum 4 weekly). Serial growth scans from 24 to 28 weeks of gestation are indicated if they have active glomerulonephritis or CKD. As mentioned previously, they should be on aspirin and venous thromboembolism prophylaxis (if indicated), their blood pressure should be strictly controlled, and they should be on pregnancy-safe medications.[18]

Treatment of active glomerulonephritides during pregnancy, de novo disease, a flare, or relapse, is difficult. Treatment will depend on severity and glomerular disease subtype (refer to disease-specific sections below). Occasionally, the diagnosis is unknown, but treatment is required; in these cases, we favor tacrolimus over high-dose steroids as this would effectively, and likely more

safely, treat minimal change disease, membranous nephropathy, focal segmental glomerulosclerosis as well as lupus nephritis.[21]

Treatment of severe flares and life- or organ-threatening disease is hugely challenging and fraught with anxiety. In these scenarios, depending on the stage of pregnancy, termination or premature delivery should be considered and discussed with the patient.

Preeclampsia is commonly encountered in women with glomerulonephritis. Preeclampsia is a clinical diagnosis, and a renal biopsy is rarely appropriate (the classic histopathological lesion is endothelial swelling "endotheliosis").[22] Nephrologists may be asked to help differentiate it from a flare of an underlying glomerulonephritis, a notoriously difficult task.[23] In some cases, serum markers may be useful; low complement levels may indicate a lupus flare or high titers of antiphospholipase A2 receptor antibodies may support a diagnosis of membranous nephropathy instead of preeclampsia. In women without CKD, the antiangiogenic factors soluble fms-like tyrosine kinase 1 and placental growth factor are likely to be useful in this situation in the future. They can be measured in serum/plasma and levels greater or lower than the manufacturer's specific cutoffs can help to diagnosed preeclampsia. They are not yet in widespread clinical practice.[24-26]

Preeclampsia can be associated with fluid overload, acute kidney injury, and oliguria. Fluid restriction/avoidance of intravenous fluids is generally recommended in preeclampsia, despite oliguria, owing to the risk of iatrogenic pulmonary edema. Diuretics are only recommended if there is pulmonary edema.[18,19,27]

SPECIFIC GLOMERULAR DISEASES

Lupus Nephritis

Lupus nephritis commonly occurs in women of childbearing age, so issues surrounding fertility and pregnancy have long been recognized as important. As a result, there are robust data on lupus nephritis and pregnancy to inform management and prepregnancy counseling. A large 2017 meta-analysis showed an increased risk of miscarriage (relative risk [RR] 1.51), prematurity (RR 3.05), small for gestational age (RR 1.59), preeclampsia (RR 1.91), hypertension (RR 1.99), and caesarean section (RR 1.85) in those with SLE compared with those without SLE. There was an increased likelihood of live birth (RR 1.38) in those without SLE.[28] A multicentre study of 71 pregnancies by Moroni et al[7,29]in which 61 women were with lupus nephritis, 56 in remission and 15 with ongoing mild activity reported an 8.4% fetal loss, 28.2% prematurity, and 16.4% small for gestational age; 19.7% had a renal flare, 8.4% preeclampsia, and 2% hemolysis, elevated liver enzymes, and low platelets syndrome.

Predicting who will have an adverse pregnancy outcome can be difficult. The study by Moroni et al[7] found that presence of antiphospholipid antibodies and arterial hypertension is associated with fetal loss. Baseline proteinuria (odds ratio [OR] 2.74), Systemic Lupus Erythematous Disease Activity Index score (a composite marker of lupus activity) (OR 1.18), active nephritis (OR 17.7), hypertension (OR 18.9), and history of renal flares (OR 5.25) all predicted prematurity as did increasing proteinuria and Systemic Lupus Erythematous Disease Activity Index score during pregnancy.

The prospective Predictors of Pregnancy Outcome: Biomarkers in Antiphospholipid Antibody Syndrome and Systemic Lupus Erythematosus study (which excluded those with proteinuria >1000 mg/24 h and creatinine >1.2 mg/dL) found the single biggest risk factor for an adverse outcome was the presence of lupus anticoagulant; however, being non-white or Hispanic and hypertensive greatly increased risk even if lupus anticoagulant negative. Given that lupus nephritis is much more common in non-white women and hypertension is very common in lupus nephritis, many women with prior lupus nephritis should be considered as having high risk of adverse pregnancy outcomes. However, most women with quiescent lupus, without significant renal impairment or proteinuria, will have good pregnancy outcomes.[30]

For most women with quiescent lupus nephritis, pregnancy does not significantly affect their estimated glomerular filtration rate (eGFR). A single-center retrospective study comparing pregnancies in women with SLE with and without lupus nephritis found no difference in eGFR between the groups at 39 months after delivery.[31] At 1-year postpartum, patients with renal flares in the cohort of Moroni et al[29] had a normal creatinine level (65.12 ± 14.08 μmol/L).

In women with known lupus nephritis, their medications should be optimized to facilitate pregnancy planning. Methotrexate and mycophenolate are contraindicated in pregnancy and should be stopped at least 6 weeks before conception to avoid teratogenicity and to ensure there is no increase in disease activity once stopped/changed to an alternative medication such as azathioprine.[32,33] If a woman conceives while taking mycophenolate, the risks should be discussed. First trimester exposure to mycophenolate is associated with congenital malformations (microtia, external auditory canal atresia, orofacial clefts, cardiovascular malformations, and digital hypoplasia) and high rates of miscarriage.[32] Management options include termination of pregnancy or immediate switch to pregnancy-safe medications. Usually mycophenolate is switched to azathioprine before pregnancy or, where appropriate, immunosuppression is stopped. A thiopurine methyltransferase level should be checked before azathioprine is started, so an appropriate starting dose can be chosen. Myelosuppression is more common in those with no or low levels of thiopurine methyltransferase activity, so a lower starting dose is usually chosen. The maximum dose to use in pregnancy is 2 mg/kg/d.[32]

Prednisolone is safe in pregnancy but is associated with diabetes, hypertension, and weight gain; ideally, they should be taking ≤ 7.5 mg/d.[32,34,35] Rituximab crosses the placenta. Rituximab exposure in the second and third trimesters lead to cord levels equal to or higher than maternal levels and neonatal B cell depletion. Long-term effects on the developing immune system are unknown.[32,36] The baby should not have live vaccinations

for 6 months after rituximab.[32] If rituximab is being used as maintenance treatment, this is often planned so a dose is given just before conception or in the first trimester.[1] All women with lupus who are pregnant should be on hydroxychloroquine. This has been shown to reduce preeclampsia,[37] disease flare,[38] fetal growth restriction,[39] and steroid exposure.[40] Tacrolimus and cyclosporine are safe to continue in pregnancy.[13]

Flares occur in 19.7-25.6%[7,41] of pregnancies. They are often diagnosed biochemically with a fall in complement levels (which tend to run higher in pregnancy), rising proteinuria, and/or a rise in creatinine. Biopsy is occasionally required. Flares are often treated with steroids (intravenous methylprednisolone and/or oral prednisolone, in combination with increasing or introducing azathioprine or tacrolimus.[32,34] For severe flares, rituximab is increasingly used (refer to discussion of risks above).[16,32] Cyclophosphamide is usually avoided but can be used in life- or organ-threatening flares.[42] Mycophenolate can be considered, for severe lupus nephritis flares, late in pregnancy as it will no longer have a teratogenic effect.[32]

Women with anti-Ro and anti-La antibodies have a risk of placental transfer of these antibodies to the fetus. This is associated with a 2-5% [43] risk of congenital heart block and a 4-16% risk of cutaneous lupus.[44,45] Hydroxychloroquine reduces the risk of congenital heart block in those with a previously affected child,[46] and low rates of congenital heart block are reported in cohorts with high levels of hydroxychloroquine use.[30] Hydroxychloroquine is recommended in all women with anti-Ro and anti-La antibodies. Fetal echocardiography is recommended from 16 weeks in women who are anti-Ro/La positive.[36]

As mentioned previously, prophylactic low-molecular-weight heparin should be given to those with antiphospholipid syndrome with previous obstetric or thrombotic complications or nephrotic-range proteinuria[1,17] and considered in those with significant proteinuria, antiphospholipid antibodies, or active lupus.

IgA Nephropathy

As IgA nephropathy (IgAN) is common and frequently affects young people,[47] it is often encountered in women of child-bearing age. Pregnancy usually proceeds uneventfully. A recent large meta-analysis found that among 820 pregnancies in 557 women, 88.3% were live births, 14.2% preterm deliveries, and 13.1% were small for gestational age; 8.6% had preeclampsia and 49.1% delivered by caesarean section. Prepregnancy renal impairment and proteinuria during pregnancy predicted prematurity, small for gestational age, and preeclampsia.[48] Pregnancy was not found to be associated with a deterioration in eGFR or an increase in renal events compared with nonpregnant women with IgAN.[48]

IgAN is a heterogeneous disease with many women entering pregnancy without significant renal impairment or proteinuria. ACE inhibition is commonly the only treatment before pregnancy; on cessation, increasing proteinuria is often noted. Treatment of IgAN during pregnancy is usually supportive, but steroids are used occasionally. Where possible, ACE inhibitors should be restarted after pregnancy. Enalapril is safe in breast feeding.[13]

MINIMAL CHANGE DISEASE

Despite commonly affecting young people, published data on minimal change disease (MCD) in pregnancy are limited. In our experience, once the disease is in remission, pregnancy proceeds uneventfully. Two older studies reported 71-76% live births.[49,50] A more recent study of 7 pregnancies in women with MCD reported 1 stillbirth (at >20 weeks) and 5 premature deliveries. Two women developed preeclampsia, and none lost renal function.[51] We would start treatment if there was nephrotic-range (or rapidly rising) proteinuria, hypoalbuminemia <25 mg/L, significant edema, or an acute kidney injury in the context of a new or known diagnosis of MCD. MCD is usually treated with steroids[52] though recent data on nonpregnant patients suggest tacrolimus can be as effective and may offer a safer alternative to high-dose steroids.[53] Either can be continued or started in pregnancy.[21,52,54] Of note, there has been a case report of an invasive mole pregnancy associated with MCD.[55]

Membranous Nephropathy

Similar to other glomerulonephritides, when in remission, pregnancy is often uneventful. One old study reported high rate of fetal loss (23%);[56] however, this has not been replicated with other studies reporting 0-11% loss.[57-60] Prematurity does appear to be common (0-33%).[56,57,60] Little is known about long-term effects on renal function. One study identified new hypertension in 9% of patients and increased proteinuria in 18% of patients at 6-month postpartum.[56] Nephrotic-range proteinuria in the first trimester was associated with adverse maternal and fetal outcomes (fetal loss, prematurity, hypertension).[56] Steroids and tacrolimus can be used in pregnancy. If rituximab is being used for maintenance, a dose should be scheduled before or early in pregnancy. We would favor treating with tacrolimus for new or relapsing disease during pregnancy.

Given the high rate of venous thromboembolism associated with membranous nephropathy, women planning pregnancy may be on anticoagulants.[61] Warfarin is associated with a high rate of miscarriage, fetal bleeding risk, and warfarin embryopathy and should be stopped within 2 weeks of missing a period.[17] Direct-acting oral anticoagulants should also be stopped in pregnancy.[62] Treatment-dose low-molecular-weight heparin is an appropriate anticoagulant in pregnancy and breastfeeding. Warfarin is safe while breastfeeding.[62]

An important case report, which provided proof of concept that human membranous nephropathy was directly due to a pathogenic antibody, demonstrated placental transfer of an alloantibody to fetal neutral endopeptidase (nephrolysin) that caused severe membranous nephropathy in the neonate without any disease in the mother.[63] We now know that the majority of "idiopathic" membranous nephropathy are due to an antibody against the phospholipase a2 receptor (PLA2R).[64]

Serum PLA2R may allow diagnosis of membranous nephropathy without biopsy in pregnancy, although a negative test does not rule out membranous nephropathy.[65] There have been 2 case reports of women with positive serum PLA2R antibodies associated with membranous nephropathy in pregnancy.[66,67] In the first case, the patient had high PLA2R titers before pregnancy and detectable titers throughout pregnancy. PLA2R antibodies were weakly positive in the cord blood. In the second case, the PLA2R was found after delivery on stored serum. Neither infant had proteinuria.

Focal Segmental Glomerulosclerosis

Although focal segmental glomerulosclerosis (FSGS) was the most common finding on biopsies performed antenatally or within a year of pregnancy,[68] there is a relative paucity of information on FSGS and pregnancy. A recent case series reported 11.8% fetal losses, 58.8% premature deliveries, 47.1% preeclampsia, and 88.2% active glomerulonephritis among 17 women with FSGS.[51] Steroids or tacrolimus can be started or continued in pregnancy; we would initiate tacrolimus if treatment was required during pregnancy. Of note, an FSGS pattern of preeclampsia has been described. This is indistinguishable from non–preeclampsia-related FSGS but disappears after delivery.[69]

ANCA-Associated Vasculitis

Pregnancies in women with active ANCA-associated vasculitis are very likely to have maternal and fetal complications, while pregnancies in those with well-controlled disease on or off treatment often proceed uneventfully. Recent studies highlight prematurity (20.4-27.8%) and small for gestational age (22.6%) in women with ANCA-associated vasculitis.[70,71] More concerning is that disease flares are relatively common, reported in 18-35% of pregnancies. Although the majority are mild-moderate flares (eg, nasal crusting, sinusitis or joint pain), severe flares (severe acute kidney injury, lung hemorrhage) have been reported. Severe flares in pregnancy are alarming, associated with up to 15% maternal death and obstetric complications (fetal loss, intrauterine growth restriction or prematurity) in up to 59%.[70,71] Starting pregnancy with active disease is also associated with very poor outcomes including maternal death.[72]

Azathioprine and steroids are safe, and methotrexate and mycophenolate are contraindicated (see previous discussion). Rituximab is increasingly used as maintenance treatment, given at a fixed interval (often 6, monthly).[73] Where possible, pregnancy should be planned to allow rituximab to be given before conception in early pregnancy (see aforementioned discussion, Lupus nephritis section). If a maintenance dose is due in the second or third trimester, we would advise holding the dose until after pregnancy but closely monitoring symptoms, ANCA titers (antimyeloperoxidase or proteinase-3 antibody levels), and lymphocyte subsets to ensure B cells remain depleted.

If someone has active disease or a rapidly progressive glomerulonephritis, they are often treated with steroids (intravenous methylprednisolone or oral prednisolone), rituximab(refer to lupus section for risks), and/or plasma exchange.[74,75] Cyclophosphamide is usually avoided but can be used in life-threatening flares or rapidly progressive glomerulonephritis.[74] Intravenous immunoglobulin has also been used.[74]

Of note, there have been rare reports of transplacental transfer of anti-MPO antibodies with neonates developing pulmonary hemorrhage and acute kidney injury necessitating immunosuppression.[72]

De Novo Glomerulonephritis During Pregnancy

The literature is scattered with case reports of de novo glomerulonephritis presenting during pregnancy. Although much depends on the glomerulonephritis in question, there are a few important general points. Preeclampsia is common in pregnancy (3-5% of the general population).[76] This is most commonly diagnosed when hypertension and proteinuria present after 20 weeks gestation and is more common closer to term.[15] Proteinuria presenting earlier in pregnancy (<20 weeks) is unlikely to be due to preeclampsia.[13] De novo glomerulonephritis in pregnancy can present with new symptomatic nephrotic or nephritic syndrome. Preexisting asymptomatic proteinuria is picked up as women routinely have their urine assessed for protein in pregnancy, often for the first time. Diagnosing the cause should be approached the same way as it would be outside of pregnancy (previous pregnancies may give clues).

Renal biopsy should only be performed if the results would change management. Complications occurred in 7% of biopsies performed during pregnancy compared with 1% after delivery in a recent systematic review.[77] All significant complications (major bleeding requiring transfusion) occurred between week 23 and 26.[77] If a biopsy is undertaken in pregnancy, it should be in the first or early second trimester.[18] As the threshold for biopsy in pregnancy is high, they are relatively rarely performed.[68] However, when planned appropriately, biopsies lead to initiation of, or change in, therapy in 66% of cases.[77] Once glomerulonephritis is diagnosed, it is usually treated as it would be outside of pregnancy (see aforementioned section) but with the limitations imposed by a smaller armamentarium of safe drugs. Women with a de novo glomerulonephritis are at high risk of maternal, fetal, and thrombotic complications. They should be managed in a specialist obstetric medicine or obstetric-renal setting.

Delivery

Timing of delivery is usually guided by obstetric factors (eg ultrasound features, presence of intrauterine growth restriction) with consideration of maternal factors such as renal function and hypoalbuminemia. A diagnosis of glomerulonephritis does not require a caesarean section although rates are higher in this population.[27] Intrapartum care of women with preexisting medical conditions has recently been the subject of the United Kingdom's National Institute for Health and Care Guidance guideline, and renal disease is specifically addressed.[27]

Postpartum

Breastfeeding is encouraged where possible. The immunosuppressants commonly used in pregnancy (steroids, azathioprine, tacrolimus, hydroxychloroquine), as well as low-molecular-weight heparin and enalapril, are all safe in breastfeeding.[13,18,78] Preeclampsia can present postnatally so blood pressure monitoring should continue postnatally. Contraception must be discussed, and long-acting reversible contraception is ideal (refer earlier discussion). It is critical to ensure appropriate follow-up is arranged. All women with preeclampsia on antihypertensives should have their blood pressure checked every 1-2 days and a medical review within 2 weeks after transfer to community care.[15] All women with glomerular disease need appropriate nephrology follow-up postnatally. The timing of this should be individualized depending on the circumstances, for example active vs quiescent disease, need for therapeutic drug monitoring, or decline in renal function during pregnancy. It is especially vital that women who present with proteinuria suspicious for intrinsic renal disease, but not formally diagnosed in pregnancy, are followed up soon after delivery – to avoid loss to follow-up and late presentation with advanced CKD owing to missed opportunities to diagnose and treat glomerulonephritis.[18] When biopsies are required, they are generally performed 4-6 weeks postpartum to allow pregnancy-related changes to resolve, provided there is no clinical urgency.[1]

Although we have described the many potential problems women with glomerulonephritis may face in pregnancy, we do not aim to discourage women, or their doctors, from considering pregnancy. Prepregnancy counseling allows women to make an informed choice about pursuing a pregnancy that is likely to be more medicalized and higher risk than the general population. With this approach (prepregnancy counseling followed by management in a multidisciplinary setting, close antenatal surveillance, and judicious use of appropriate medications), many women have successful pregnancies. Although we treat all of these pregnancies as high risk with increased surveillance, many turn out to be uneventful with a normal delivery of a healthy baby. Looking after women before and during these pregnancies, although sometimes challenging, is very rewarding.

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