

Obstetric Nephrology: Pregnancy and the Kidney—Inextricably Linked

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Summary

This issue's Moving Points highlights the challenges and victories of a subspecialty within nephrology, obstetric nephrology. This article presents an overview of the renal physiology of normal pregnancy and exciting new developments in the understanding of both common renal disorders, such as lupus nephritis, diabetic kidney disease, and preeclampsia, and less common but life-threatening disorders, such as thrombotic microangiopathies.

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Healthy Kidneys, Healthy Pregnancy

A healthy pregnancy, one in which a baby is born at term with minimal untoward physical consequences to the mother, is the ideal outcome. Indeed, when it occurs, it is nothing short of a miracle. That the maternal kidneys are such important players in this process is perhaps not news to the seasoned nephrologist, but it is a concept that bears emphasizing, particularly when a woman with kidney disease or, even hypertension, contemplates pregnancy.

Why this should be so is probably a result of the critical role of the kidneys in adapting the circulation to the increasing demands of the conceptus and accommodating the alterations in blood flow that are necessary for the rapidly enlarging uterus, the growing placenta, and, of course the fetus. Fertility is not significantly impaired until renal function is severely reduced—and even then, many pregnancies occur after women have already initiated renal replacement therapy. Thus, the nephrologist is often involved in the care of women with all forms of kidney disease that afflict women in their childbearing years.

Obstetric nephrology is truly an interdisciplinary effort, and good outcomes are contingent on collaboration among obstetricians, nephrologists, rheumatologists, and endocrinologists. Scientific advances in this field are published in journals that span all of these disciplines. This Moving Points in Nephrology focuses on obstetric nephrology, with the goal of bringing together some of the important, clinically relevant issues that nephrologists involved in the care of pregnant women need to be aware of.

The important physiologic adaptations to normal pregnancy are discussed by Drs. Odutayo and Hladunewich in their review of renal hemodynamic and metabolic physiology in normal pregnancy. They address alterations in tubular and glomerular function, particularly the determinants of the pregnancy-associated increases in GFR and renal blood flow. Familiarity with these changes is critical for accurately interpreting laboratory results in the pregnant woman, in

whom BUN, creatinine, serum sodium, and bicarbonate are usually slightly lower than in nonpregnant women.

It is difficult to practice nephrology without being familiar with all aspects of the care of patients with diabetes. This is certainly true in pregnancy, and Drs. Mathiesen, Ringhom, Feldt-Rasmussen, Clausen, and Damm provide a comprehensive and innovative approach to treating pregnant women with diabetes. They emphasize, with data from their own clinical experience, the importance of metabolic and BP control in minimizing pregnancy-associated complications, such as worsening of nephropathy, preeclampsia, and preterm birth. Such careful monitoring has resulted in successful pregnancy outcomes that are close to 95%–100%. This is quite remarkable, especially given the prohibition of renin-angiotensin system blockers during gestation.

The challenges of managing lupus nephritis are well known to most nephrologists. Drs. Stanhope, White, Moder, Smyth, and Garovic provide a scholarly review of the important issues, including the immune alterations that may play a role in pregnancy-exacerbated complications, such as the possible role of decreased CD4+/CD25+ regulatory cells in superimposed preeclampsia. That women with lupus who become pregnant are particularly at risk for disease flares may be related to the hormonal changes of pregnancy—in particular elevations in estrogen levels. The authors review factors associated with poor outcomes, including their own data from the Mayo Clinic, and provide an up-to-date approach for managing these complex situations.

Thrombotic microangiopathy during or after pregnancy is fortunately uncommon, but pregnancy is clearly a trigger for both thrombotic thrombocytopenic purpura and hemolytic uremic syndrome. These disorders present particular diagnostic challenges during pregnancy because the clinical and laboratory abnormalities overlap with those of the hemolysis elevated liver enzymes low platelet (HELLP) variant of preeclampsia and acute fatty liver of pregnancy.

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Drs. Fakhouri, Vercel, and Freneaux-Bacchi review the current landscape of AKI in pregnancy, with an update on the pathophysiology of the microangiopathic syndromes that nephrologists encounter in pregnancy. They classify thrombotic microangiopathy on the basis of pathogenic mechanisms and emphasize the importance of elucidating mechanisms in order to provide appropriate treatment. For example, the appreciation of the role of complement alternative pathway dysregulation in the pathogenesis of atypical hemolytic uremic syndrome offers the possibility that this devastating pregnancy-associated illness can be prevented or treated with anti-C5-blocking antibody (eculizumab).

Last but not least, Dr. Umans, a seasoned obstetric nephrologist, provides a nephrologist's perspective on preeclampsia, the hypertensive disorder unique to pregnancy that is a leading cause of maternal and fetal death worldwide. He reviews the newest information on pathogenesis and discusses the role of angiogenic factors in the renal and systemic manifestations of the disease. He puts these observations into a therapeutic perspective and reminds us that much more translational work needs to be done. We hope that this Moving Points section will stimulate the nephrology community to consider the nephrologic aspects of obstetrics and generate more research in this critically important area.