Chronic Kidney Disease and Pregnancy

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Summary: Women with chronic kidney disease (CKD) are at risk for adverse pregnancy-associated outcomes, including progression of their underlying renal dysfunction, a flare of their kidney disease, and adverse pregnancy complications such as preeclampsia and preterm delivery. Earlier-stage CKD, as a rule, is a safer time to have a pregnancy, but even women with end-stage kidney disease have attempted pregnancy in recent years. As such, nephrologists need to be comfortable with pregnancy preparation and management at all stages of CKD. In this article, we review the renal physiologic response to pregnancy and the literature with respect to both expected maternal and fetal outcomes among young women at various stages of CKD, including those who attempt to conceive while on dialysis. The general management of young women with CKD and associated complications, including hypertension and proteinuria are discussed. Finally, the emotional impact these pregnancies may have on young women with a chronic disease and the potential benefits of care in a multidisciplinary environment are highlighted.

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Women with underlying renal disease are among the highest-risk patient populations for adverse maternal and fetal outcomes. Because the kidneys play such a significant role in the maternal accommodation to pregnancy, pregnancy-associated risks increase along with the stage of chronic kidney disease (CKD). Pregnancy is safer when women have only mild renal insufficiency as opposed to advanced renal dysfunction, and when associated hypertension and proteinuria are well managed and controlled. As such, nephrologists should be involved actively in pregnancy planning to assist young women with all types and stages of CKD find the optimal time to consider conception, to provide reproductive counselling, and to carefully prepare them for pregnancy.

In this article, we review the renal physiologic response to pregnancy and the literature with respect to both expected maternal and fetal outcomes in women at various stages of CKD, including those who attempt to conceive while on dialysis. Disease-specific reviews occur in other sections of this special issue. The general management of young women with CKD and associated complications, including hypertension and proteinuria are discussed. Finally, the emotional impact these pregnancies may have on young women with a chronic disease and the potential benefits of care in a multidisciplinary environment are highlighted.

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PHYSIOLOGICAL ADAPTATION TO PREGNANCY

A healthy pregnancy requires significant structural, hemodynamic, and renal adaptations to ensure a successful outcome. These alterations, which are noted to begin as early as 6 weeks after conception, include dilatation of the urinary collecting system (calices, renal pelvis, and ureters), a decrease in systemic vascular resistance, as well as a remarkable increase in renal plasma flow (RPF), and hence, the glomerular filtration rate (GFR). Alterations in an array of hormones that govern both vasodilatation and vasoconstriction, including but not limited to nitric oxide, endothelin, and relaxin, as well as alterations to mediators of the renin-angiotensin-aldosterone system (RAAS), are responsible for the maternal accommodation to pregnancy, and the net effect of the pregnancy-associated physiological adaptation includes a vasodilated state. Maternal systemic vascular resistance decreases significantly, leading to a decrease in mean arterial pressure, which typically will decrease in the first trimester of pregnancy to reach a nadir by approximately 18 to 24 weeks' gestation, before returning back to baseline closer to term.[1,2] The resulting decreased afterload contributes to the increase in cardiac output that is characteristic of a healthy human pregnancy. In parallel, increments in renal hemodynamic function are notable with an increased RPF and an augmented GFR.

Glomerular Physiology

Glomerular hyperfiltration is the most notable physiological adaptation to a healthy pregnancy, which is

manifested clinically by a decrease in the serum creatinine level. Both studies in animal models and human physiologic assessments have provided some insights into the key factors that contribute to the increments in the GFR, represented by the following equation:

$$GFR = \kappa_f \times (\Delta P - \pi_{GC})$$

where ΔP is the transcapillary hydraulic pressure difference or the pressure generated across the glomerulus; π_{GC} is the mean glomerular intracapillary oncotic pressure, the force that opposes the formation of glomerular filtration; and K_f is the glomerular ultrafiltration coefficient (ie, the product of the surface area available for filtration and the permeability to ultrafiltrate across the three layers of the glomerulus).[3]

In animal models at least, these physiological changes occur irrespective of the presence of underlying kidney damage without any measured increase in intraglomerular pressure (ΔP), as shown in an array of studies that used elegant micropuncture techniques for direct pressure measurements.[4–7] Even in the presence of severely reduced renal mass, there is no evidence of increased intraglomerular pressure (ΔP).[8] Unfortunately, there is an extreme paucity of studies to better illuminate these necessary physiological processes in healthy young women, and none in women with varying degrees of renal insufficiency. Odutayo and Hladunewich[9] previously conducted a systematic review of all studies performed in human pregnancy that used either inulin or iothalamate and p-aminohippurate clearance methodology to assess GFR and RPF at different time points during gestation in relation to a baseline or control group. Studies identified were limited and difficult to compare because all were performed at different time points in gestation with significant differences in study methodology, including differences in patient positioning (semisupine, recumbent, sitting, and left lateral decubitus), inconsistent use of bladder catheterization, and different methods to correct for body surface area.

Irrespective of these methodologic issues, our best understanding of the renal physiological accommodation to pregnancy includes an early gestational increase in both RPF and GFR above nongravid levels, with the former slightly surpassing the latter (41% and 37%, respectively). GFR remains increased until approximately a week postpartum, whereas RPF gradually decreases throughout pregnancy. Consistent with these changes, the filtration fraction decreases slightly in early pregnancy, but then increases consistently throughout pregnancy and remains increased in the early postpartum period (Fig. 1, Table 1). It has been suggested that the increase in GFR is solely a product of increments in RPF in the first and second trimesters,[10] but given the decrease in renal plasma flow in the later half of pregnancy and early postpartum, other changes must account for the maintenance of GFR. Without the ability to directly measure the determinants of GFR, one can only speculate that modest increments in either ΔP, K_f, or both are required because sufficient decrements in oncotic pressure have been excluded as the principal mechanism.[11] All values normalize between weeks 6 and 8 postpartum.[12]

Proteinuria

Alterations in the tubular handling of glucose, amino acids, and uric acid also have been noted in healthy human pregnancies, but the most clinically relevant are the changes noted in protein excretion, which often is attributed to hyperfiltration. In pregnancy, significant protein excretion usually is defined as 300 mg or more

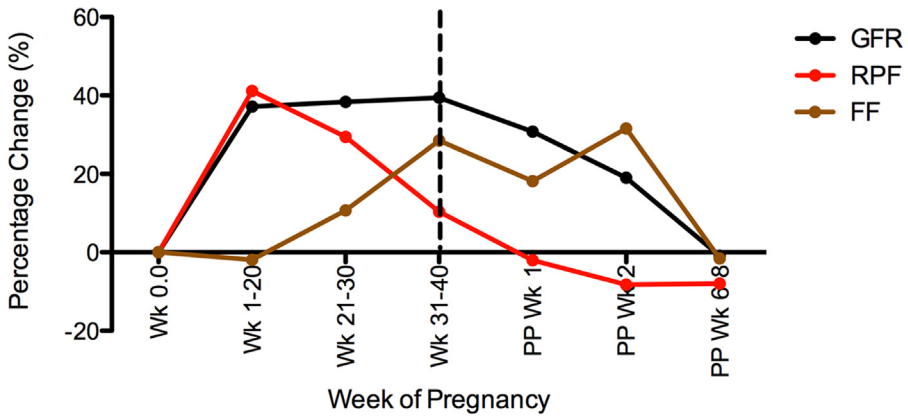

Figure 1. Increments in GFR, RPF, and filtration fraction (FF) as measured by inulin or iothalamate and p-aminohippurate clearance methodology, respectively, at different time points during gestation. Reprinted with permission from Odutayo and Hladunewich.[9]