

## **PCL/18/03 - update October 2020**

Globally, chronic kidney disease (CKD) is a huge and growing health problem. Some risk factors for CKD are well established, for example hypertension and diabetes. Targets for blood pressure control exist as there is good evidence that meeting blood pressure targets can help keep someone with or without CKD healthy. However, there are a number of other potential risk factors for CKD that are much less well understood, but that could be very important. One such factor is what influence a woman's maternal and child rearing history might have on her risk of CKD and future kidney health.

Gender differences exist in the pathogenesis and progression of CKD. Before the age of 60, CKD is less common in women than it is in men. However, beyond the age of 65, the prevalence of CKD is greater in women, suggesting a potential role for reproductive hormones in attenuating CKD risk. Reproduction itself is a well-established risk factor for maternal acute kidney injury and more recently complications of pregnancy including pre-term birth, gestational hypertension, diabetes and pre-eclampsia have been demonstrated to be risk factors for future end stage renal disease. However, little is known about what effect an uncomplicated pregnancy has on future CKD risk.

A number of profound and complex physiological changes occur to the renal system during pregnancy. These changes include a 50-85% increase in renal blood flow, a 50% increase in glomerular filtration rates, afferent and efferent arteriole dilation, pelvicalyceal dilation, hydronephrosis, increased glomerular basement membrane size, and substantial alterations in tubular function. There are also significant hormonal and systemic changes with increased renin-angiotensin-aldosterone system (RAAS) activation and reduced sensitivity to RAAS, leading to increased water retention and reduced plasma osmolality.

Little is known about what effect these extensive physiological changes might have on a women's future kidney health. The potential impact of these changes could be particularly important to women who are multi-parous or who have multiple (twin or more) births. At present it is not clear if women who have a greater number of pregnancies are at increased risk of future CKD or indeed end stage renal disease, even if these pregnancies are uncomplicated. Similarly, with an ageing obstetric population it is of interest as to whether or not maternal age at time of delivery impacts upon future CKD risk.

During my CSO project I will use the UK Biobank data resource to examine the influence of maternal history and other lifestyle factors on the future risk of CKD development and progression. The UK biobank is a unique resource as it holds an unprecedented amount of data on over 5 00,000 participants aged 40-69 recruited between 2006 and 2010 throughout the UK. Participants have consented to the use

of their data for health-related research and the information available is comprehensive making it an ideal resource to use to address these unanswered questions about a women's reproductive history and their future kidney health. During these uncertain time with COVID-19 an added attraction of this project is that work can be done remotely and there is no need for further patient recruitment or contact, thus reducing burdens on participants and maximising use of existing excellent resources.