Hot Off the Press : Basic Science

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(Pictured from left to right)

Subclinical First Trimester Renal Abnormalities Are Associated With Preeclampsia in Normoalbuminuric Women With Type 1 Diabetes.

Kelly CB, Hookham MB, Yu JY, Jenkins AJ, Nankervis AJ, Hanssen KF, Garg SK, Scardo JA, Hammad SM, Menard MK, Aston CE, Lyons TJ / Diabetes Care. 2017 Nov doi: 10.2337/dc17-1635

This is a somewhat provocative manuscript published in Diabetes Care just last month.

Preeclampsia is a common cause of maternal and infant morbidity and mortality in pregnancy[1]. Its prevalence is higher in women with type 1 diabetes and is associated with increased risk of renal disease later in life[2].

In this study by Kelly and colleagues, the authors examined markers of subclinical renal injury and the relationship with development of preeclampsia in normoalbuminuric women with type 1 diabetes[3]. The authors focused on two biomarkers of tubular injury: Kidney Injury Molecule -1 (KIM-1) and neutrophil gelatinase-associated lipocalin (NGAL) as well as estimated GFR as determined by CKD-epi.

Interestingly, urinary NGAL, was significantly increased at first visit (~12 weeks) in women with diabetes who developed preeclampsia when compared with those women who did not. By contrast, neither plasma NGAL or urinary KIM-1 were associated with preeclampsia. In addition, eGFR was increased at first visit in women who developed preeclampsia compared with those who did not.

The difference in eGFR is perhaps not surprising as it is reflective of glomerular hyperfiltration and glomerular stress. Given the well-established microalbuminuria in preeclampsia this has long been appreciated as a glomerular disease. As such, association of early hyperfiltration (beyond what is typically seen in normal pregnancy) with subsequent development of preeclampsia is perhaps not surprising. Nevertheless changes in GFR may have value in risk assessment in early pregnancy.

Perhaps more surprising is the elevation in NGAL in those who developed preeclampsia. NGAL is better known as a marker of damaged epithelial cells, largely in ischemic and nephrotoxic injury. Based on their observations, the authors propose a prediction model for development of preeclampsia which incorporates urinary NGAL and observed an improved predictive value compared to models based on only clinical factors. Tubular injury is not typically considered a hallmark of preeclampsia so changes to urinary NGAL and utility in prediction of preeclampsia are surprising. It is notable that no changes were seen in a separate tubular injury marker KIM-1.

A number of caveats must also be considered. First, the study focused exclusively on women with diabetes and findings may not extend to healthy individuals or to other conditions. Second, the number of patients studied was low. Third, there were some baseline differences between women with type 1 diabetes who developed preeclampsia and those who did

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not. Finally, the discrepancy between KIM-1 and NGAL results is curious, although in the manuscript the authors suggest that KIM-1 has weaker prognostic value than NGAL. All limitations are acknowledged by the authors and they correctly advocate for large international collaborations to validate early studies such as this.

Nevertheless, the present study does highlight a potential role for subclinical renal injury in predisposing women with type 1 diabetes to preeclampsia. In addition, this early work sets the stage for larger investigations to determine whether incorporation of NGAL into current models can improve risk prediction for preeclampsia.

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Hot Off the Press

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Blood pressure lowering and outcome according to baseline blood pressure

Many guideline recommendations for hypertensive patients favour a target for treatment in most patients to a systolic blood pressure of less than 140 mm Hg. Furthermore, systematic reviews and meta-analyses suggest that more intensive treatment is beneficial compared to less intensive treatment [1,2]. There is less agreement on how far systolic blood pressure should be reduced. While results from recent reviews and meta-analyses [3-5] suggest that a target systolic blood pressure of approximately 130 mm Hg in high-risk cardiovascular patients may be optimal, the benefit for hypertensive patients in primary prevention and with less risk remains more uncertain.

Recently, Brunström and Carlberg [6] performed a study that may help to increase our understanding on these issues. The authors performed a systematic review and meta-analysis on the association of blood pressure lowering with cardiovascular morbidity and mortality across different baseline systolic blood pressure levels to assess the optimal cut-off for treatment of hypertension. The authors included trials with 1000 or more patient years of follow-up that compared antihypertensive drug treatment versus placebo, or compared one drug treatment with different target blood pressure values. Studies comparing different drug classes were not included, and excluding studies in patients with heart failure or left ventricular dysfunction and in patients with a recent myocardial infarction. Brunström and Carlberg eventually included 74 trials with 306 273 participants (40 % women, mean age 64 years). The majority, 51 studies including 192 795 patients (47 % women, mean age 63 years), were considered primary preventive, while the remaining trials were considered secondary preventive, mostly in coronary heart disease or stroke patients.

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