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P239 -Clinical, Angiogenic and Immune System Markers Predict Pre-Eclampsia in Women with CKD During Pregnancy

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Introduction and Aims:
Pre-eclampsia (PE) complicates over 20% of pregnancies in women with CKD and is associated with substantial maternal and fetal morbidity. In healthy women, PE is associated with immune activation and altered circulating angiogenic factors (with elevated soluble FMS-like tyrosine kinase-1/placental growth factor or sFLT-1/PlGF ratio). There are currently limited data in pregnant women with CKD.
The aims of this study were to assess longitudinal changes of markers inflammation, immunity and angiogenic factors during pregnancy in women with CKD and to assess their relationship to the development PE.
Methods:
Women with CKD were recruited from a tertiary renal-obstetric antenatal clinic in Birmingham, UK between 2011 and 2016. Baseline demographics, serial serum samples and pregnancy outcomes were recorded. Samples were analysed for IgG/A/M, high-sensitivity CRP, serum free light chains (sFLC), Beta-2 Microglobulin (B2M), complement factors 3 & 4 (C3/4), uric acid (UA), creatinine, cystatin-C and sFLT-1/PlGF using the Roche Cobas® platform.
Multivariable analysis was performed to identify demographic factors that were independently associated with PE. Trends in biomarkers over time were assessed using regression models with a generalised estimating equation approach. Predictive accuracy of the biomarkers at gestations <16, 16-21, 22-27, 28-31 & 32+ weeks was then assessed using ROC curves. Correlations between markers were assessed using Spearman's rho, and Wilcoxon's tests were used for ante/postnatal sample comparison.
Results:
164 pregnancies (136 women), contributing to 398 samples were analysed. Pre-pregnancy CKD stage was 1 (39%), 2 (36%), 3 (23%) and 4 (2%). PE was diagnosed in 23% of pregnancies, with rates increasing with CKD stage (17% vs. 45% for CKD 1 vs. 3-4, p=0.011). Multivariable analysis found and the risks of PE to be significantly higher in women of White ethnicity (OR 5.89, p=0.002), non-smokers (OR 11.11, p=0.006), those with Systemic Lupus Erythematosus (OR 6.48, p=0.015), chronic hypertension (OR 7.95, p<0.001) or a previous pregnancy with PE (OR 4.20, p=0.036).
Concentrations of sFLC, B2M, serum creatinine, cystatin-C & UA increased significantly over the antenatal period, being significantly higher in women who developed PE. The greatest predictive accuracy for PE was observed at 16-21 weeks, for sFLC and cystatin-C (AUROC 0.745, 0.810 respectively). The rate of antenatal change differed significantly for two serum markers; with C3 levels increasing more rapidly (p<0.001) and IgA concentrations falling more quickly (p=0.015) in the PE vs. non-PE group.
The sFlt-1/PlGF ratio was predictive for the subsequent development of PE at 22-27 weeks gestation (mean: 4.9 vs. 2.7, AUROC=0.728, p=0.005), but not earlier or later gestations (figure 1), and was weakly correlated with serum creatinine levels (rho=0.176, p=0.002). sFLt-1 and PlGF levels decreased significantly from pre- to post-delivery (p<0.001), from (median) 2370 pg/ml to 92 and 423 to 12, respectively.
Conclusions:

In women with CKD, an elevated sFLT-1/PlGF ratio is predictive of PE at 22-27 weeks gestation, but not earlier or later gestations. Its predictive accuracy is comparable to that of markers of kidney function, sFLC and B2M levels. Angiogenic factor levels during pregnancy may be related to baseline renal function.