Low nephron endowment and renal maladaptation to pregnancy as possible pathogenetic mechanism of preeclampsia

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DOI: 10.36129/jog.2024.S23

Objective. We evaluated the association of serum creatinine (sCr) during the I trimester of pregnancy and preeclampsia (PE) based on the theoretical hypothesis that PE is a clinical expression of poor nephron endowment with the inability of kidneys to meet the increased functional demands of pregnancy, for the followings reasons: 1) renal patients (including solitary kidney) are at increased risk of PE; 2) most patients with PE are healthy before and after pregnancy; 3) the recurrence of PE in families and subsequent pregnancies; 4) the increased risk of hypertension and renal insufficiency later in the life of PE patients.

Materials and Methods. Fifty-two women with PE and 49 normal pregnancies with normal renal function, were studied. We calculated (univariate logistic regression) the PE odds ratio (OR) according to sCr during pregnancy.

Results. We found a strong positive association between sCr at I trimester and PE (OR 1.2 per mmol/L of sCr, 95%CI 1.1-1.3, $p < 0.0001$). The corresponding AUC of the ROC curve was 0.85 (95%CI 0.77-0.94). Using 50 mmol/L as the cut-off, sensitivity was 0.79 (95%CI 0.66-0.88) and specificity 0.94 (95%CI 0.83-0.99).

Conclusions. SCr in the I trimester, although in the normal range, was strongly associated with PE. The higher risk of PE for sCr > 50 mmol/L (0.57 mg/dL) may be due to the reduced renal functional reserve related to low nephron endowment with a consequent maladaptation to the increased pregnancy-related functional demand. The increase in blood pressure and proteinuria might be due to sub-optimal renal clearance of placental-derived metabolites toxic to the endothelium. SCr measured early in pregnancy may be a promising predictive marker of PE.