APOL1 in an ethnically diverse pediatric population with nephrotic syndrome: implications in focal segmental glomerulosclerosis and other diagnoses

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Abstract

Background *APOL1* high-risk genotypes (HRG) are associated with increased risk of kidney disease in individuals of African ancestry. We analyzed the effects of *APOL1* risk variants on an ethnically diverse Brazilian pediatric nephrotic syndrome (NS) cohort.

Methods Multicenter study including 318 NS patients, categorized as progressors to advanced CKD [estimated glomerular filtration rate (eGFR)] < 30 mL/min/1.73 m^2] and slow/non-progressors (eGFR $\geq$ 30 mL/min/1.73 m^2 through the study). We employed Cox regression with progression time as the outcome and *APOL1* genotype as the independent variable. We tested this association in the entire cohort and three subgroups; (1) focal segmental glomerulosclerosis (FSGS), (2) steroid-resistant NS (SRNS), and (3) those who underwent kidney biopsy.

Results Nineteen patients (6%) had an HRG. Of these, 47% were self-reported White. Patients with HRG manifested NS at older ages and presented higher frequencies of FSGS and SRNS. HRG patients progressed to advanced CKD more often than low-risk-genotype (LRG) children in the whole NS cohort ($p = 0.001$) and the three subgroups. In SRNS and biopsied patients, a single risk variant was associated with trends of higher CKD progression risk.

Conclusions Novel discoveries include a substantial prevalence of HRG among patients self-reported White, worse kidney outcomes in HRG *versus* LRG children in the FSGS subgroup, and a trend of higher CKD progression risk associated with a single risk variant in the SRNS cohort. These findings suggest *APOL1*-associated NS extends beyond patients self-reported non-White, the HRG effect is independent of FSGS, and a single risk variant may have a detrimental impact in children with NS.

Keywords *APOL1* · Risk alleles · Nephrotic syndrome · Focal segmental glomerulosclerosis · Children · Brazilian admixture race