Effect of a Single Apolipoprotein L1 Gene Nephropathy Variant on the Risk of Advanced Lupus Nephritis in Brazilians

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Hello, my name is Gisele Vajgel. I'm a nephrologist here in the Hospital das Clinicas of the Federal University of Pernambuco, and on behalf of my coauthors, I'm going to present our study that was recently published in *The Journal of Rheumatology*. The title of the study is "Effect of a Single Apolipoprotein L1 Gene Nephropathy Variant on the Risk of Advanced Lupus Nephritis in Brazilians."

Since 2010, it's well known that endstage renal disease is more prevalent among African Americans due to the presence of *APOL1* renal risk variants. However, the impact of those variants in mixed ancestry population is unclear. The Brazilians are a mixed population with different proportions of Amerindian, African, and European ancestry.

In Brazil, we have few studies that genotyped *APOL1*. Lupus nephritis (LN) is the main reason for nondiabetic kidney biopsy according to the Pernambuco Registry of Glomerulonephritis disease. Pernambuco is our state in northeastern Brazil.

The primary hypothesis of our study was to determine whether there was an association between *APOL1* renal risk variance and the development of progressive chronic kidney disease (CKD) defined as a sustained estimated glomerular filtration rate < 30 mL/min/1.73 m^2.

Secondary analysis assessed the impact of *APOL1* renal risk variance on additional kidney outcomes in LN, including kidney histology and long-term kidney function.

Patients with LN were enrolled from 3 outpatient clinics from Brazil, specializing in the treatment of glomerulonephritis. Two of them were in Recife, northeast of Brazil, including Hospital das Clinicas in the Federal University of Pernambuco, where we are right now, and one in São Paulo, southeastern Brazil.

We genotyped *APOL1* G1 and G2 risk alleles in 201 non-White Brazilians with LN and in 222 healthy controls. We did not include patients with non-LN histologic patterns, including those with collapsing glomerulopathy. Genomic DNA was isolated from whole blood and shipped to Wake Forest University, School of Medicine for *APOL1* genotyping using Taqman asssays.

There were no different frequencies of *APOL1* allele between LN cases and controls. Only 4 cases with LN had 2 risk alleles. The groups were analyzed based on the presence of G1 or G2 alleles. The groups had similar baseline clinical and demographic characteristics, eGFR, proteinuria, and histologic class of LN.

However, we noticed that the initial biopsy from patients with 1 or more renal risk variance had more chronic damage compared with those with zero. They had more glomerular sclerosis, tubular atrophy, interstitial fibrosis, and also higher chronicity index.

In this table [i.e., 3:24 in video], we can see that those with 1 or more renal risk variance had more CKD stage 4 and stage 5. Also, the time from initial diagnosis of LN to endstage renal disease was significantly shorter in LN cases with 1 or more risk alleles compared to those with zero.

Here [i.e., 3:48 in video] we can see the Kaplan-Meier survival curves for CKD and endstage renal diseases with significant *P* values.

This table [i.e., 3:57] displays the outcomes in the 4 LN cases with 2 *APOL1* risk alleles. Despite this small sample, half of them progressed to CKD stage 4 and one had persistent proteinuria after 3 rounds of induction therapy.

The low frequency of *APOL1* to risk allele carriers in our Brazil lupus cohort did not permit performance of outcome analysis using the traditional autosomal recessive model. However, the presence of even 1 allele demonstrates a significant association with advanced CKD during follow-up.

Moreover, this dose-dependent cytotoxicity has been shown by all the authors, including individual studies.

It's important to mention that the presence of the genetic variants *per se* not preclude clinical disease. A second heat or another influence should be there to trigger the disease and the risk for CKD. HIV and lupus are strong influences as these are conditions that produce high loads of interferon, which stimulates the cellular expression of *APOL1*.

We conclude that frequencies of *APOL1* renal risk variance in non-White Brazilians with LN are not significantly different from those in healthy non-White Brazilians. But participants with ≥ 1 *APOL1* renal risk variance had more severe kidney disease at presentation and higher stages of CKD after therapy compared to those with zero *APOL1* renal risk variance.

And finally, I'd like to thank my co-authors for great help and for this opportunity.