End-stage renal disease in African Americans with lupus nephritis is associated with APOL1.

OBJECTIVE: Lupus nephritis (LN) is a severe manifestation of systemic lupus erythematosus (SLE) that exhibits familial aggregation and may progress to end-stage renal disease (ESRD). LN is more prevalent among African Americans than among European Americans. This study was undertaken to investigate the hypothesis that the apolipoprotein L1 gene (APOL1) nephropathy risk alleles G1/G2, common in African Americans and rare in European Americans, contribute to the ethnic disparity in risk.

METHODS: APOL1 G1 and G2 nephropathy alleles were genotyped in 855 African American SLE patients with LN-ESRD (cases) and 534 African American SLE patients without nephropathy (controls) and tested for association under a recessive genetic model, by logistic regression.

RESULTS: Ninety percent of the SLE patients were female. The mean ± SD age at SLE diagnosis was significantly lower in LN-ESRD cases than in SLE non-nephropathy controls (27.3...
± 10.9 years versus 39.5 ± 12.2 years). The mean ± SD time from SLE diagnosis to development of LN-ESRD in cases was 7.3 ± 7.2 years. The G1/G2 risk alleles were strongly associated with SLE-ESRD, with 25% of cases and 12% of controls having 2 nephropathy alleles (odds ratio [OR] 2.57, recessive model P = 1.49 × 10(-9)), and after adjustment for age, sex, and ancestry admixture (OR 2.72, P = 6.23 × 10(-6)). The age-, sex-, and admixture-adjusted population attributable risk for ESRD among patients with G1/G2 polymorphisms was 0.26, compared to 0.003 among European American patients. The mean time from SLE diagnosis to ESRD development was ~2 years earlier among individuals with APOL1 risk genotypes (P = 0.01).

**CONCLUSION:** APOL1 G1/G2 alleles strongly impact the risk of LN-ESRD in African Americans, as well as the time to progression to ESRD. The high frequency of these alleles in African Americans with near absence in European Americans explains an important proportion of the increased risk of LN-ESRD in African Americans.

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