Abstract citation ID: gfae069.588

#832
Sickle cell trait and APOL1 high risk genotype increase the risk of ESKD similar to diabetes in British Africans

University of Exeter, United Kingdom

Background and Aims: Little is known of the risk of end-stage kidney disease (ESKD) in British Africans with Sickle Cell Trait or APOL1 High-risk genotypes. We aim to determine the prevalence of the APOL1 high-risk genotype and genetically defined Sickle Cell Trait in British Africans and their association with ESKD.

Method: We analysed 7380 British Africans from a UK population cohort, UK Biobank. It contains deep phenotypes, biomarkers, and DNA sequence data. We used whole exome sequencing data to identify carriers of known APOL1 high risk genotypes (G1G1, G1G2, G2G2) and SCT (heterozygous carriers of p.Glu7Lys in HBB). We identified individuals with ESKD (in receipt of renal replacement therapy including kidney transplant) using self-report, hospital admissions records, and general practice records. We used a cox proportional hazard model to determine the risk of ESKD with these genotypes adjusted for age, sex, hypertension, smoking and diabetes.

Results: 1131/7380 (17.9%) British Africans carry the APOL1 High risk genotype whereas 860/7380 (14.3%) had genetically defined SCT. Both risk states were found in 216/7380 individuals. Together, 32.2% carry one or both of these variants and 36/2207 (1.6%) developed ESKD. Of those with neither SCT nor APOL1 HR genotype 32/5173 (0.67%) developed ESKD.

The multivariable cox-proportional hazard model showed that APOL1 high risk genotype increased the risk of ESKD by two-fold (HR 2.12-95% CI 1.19-3.79), \( p = 0.011 \). Surprisingly, the risk of ESKD was also two-fold higher in SCT carriers (HR 2.59 95% CI 1.44-4.68), \( p = 0.002 \) independent of APOL1 genotype. This risk was of ESKD for people with either SCT or the APOL1 high risk genotype was similar to that associated with diabetes (HR 2.75 95% CI 1.58-4.80), \( p < 0.001 \).

The polygenic score for eGFR did not change the risk of ESKD in these carriers.

Conclusion: We show for the first time that 1 in 3 British Africans carry either two APOL1 high-risk variants or sickle cell trait, both of which double the risk of ESKD. These genetic risk factors increase the risk of developing ESKD to a level similar to that resulting from diabetes. A sensible starting point would be a trial of screening and aggressive management of conventional risk factors for ESKD.