Gene linked to worsening kidney disease in African-Americans

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In African Americans with kidney disease related to hypertension (high blood pressure), a common gene variant is associated with a sharply increased risk of progressive kidney disease, according to a study presented at the American Society of Nephrology's 43rd Annual Meeting and Scientific Exposition. End Stage Renal Disease (ESRD) associated with hypertension occurs in the African American population at a rate 13.1 times greater than that of their white counterparts.

"We found that individuals with the common genotype were approximately 1.5 times more likely to have progressive kidney disease than those with other genotypes," comments Brad C. Astor, PhD (Johns Hopkins Bloomberg School of Public Health, Baltimore). The variant gene—found in more than half of patients in the study—could contribute to the high rate of ESRD among African Americans.

The researchers performed genetic studies to identify variant forms of the gene MYH9 in 706 African Americans with kidney disease related to high blood pressure (hypertensive nephrosclerosis). The patients were drawn from a larger study, the African American Study of Kidney Disease and Hypertension (AASK).

"African Americans are at much higher risk of ESRD compared to white Americans, but the reasons for this discrepancy are unknown," Astor explains. "A genetic variation of the MYH9 gene, common in African Americans, was recently found to be associated with ESRD in individuals without diabetes. We examined the association between this

genetic variation and progression of kidney disease in African Americans with hypertensive nephrosclerosis."

In the AASK patients, several MYH9 gene variants were related to the risk of decreased kidney function or ESRD. Participants with one MYH9 variant were likely to have other variants as well.

The same MYH9 gene variant previously linked to nondiabetic ESRD was also associated with an increased risk of progressive kidney disease in the AASK patients. The risk of death, ESRD, or a significant drop in kidney function was 50 percent higher than in those without the variant gene.

The variant MYH9 gene was very common, present in 55 percent of the AASK study participants. Its association with progressive kidney disease was independent of age, sex, or treatment for high blood pressure. The same variants are present in many African Americans without kidney disease, however.

The results add new evidence linking MYH9 variants to racial differences in kidney disease rates and outcomes. "Associations between specific genetic variations and outcomes can help us understand the pathophysiologic processes involved in progressive kidney disease and may lead to areas of research to slow or prevent progressive kidney disease," says Astor.

Meanwhile, newer studies raise questions about the significance of the MYH9 variants.* Those studies suggest that a neighboring gene, called APOL1, may actually be the causal gene for non-diabetic ESRD/CKD in African Americans. MYH9 may simply be a marker of the causal gene. Further studies are needed to dissect the contribution of APOL1 and MYH9 in CKD in African Americans and to determine the utility of the APOL1/MYH9 locus in diagnosis and patient management.

Astor points out that the AASK study, designed to test different blood pressure medications and blood pressure goals, had strict inclusion and exclusion criteria. "The results in this study may not be generalizable to other populations," he notes.

Provided by American Society of Nephrology