Study: Non-genetic factors play role in non-diabetic kidney disease among African-Americans

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The high rate of non-diabetic kidney disease in African-Americans is strongly associated with variations in a particular gene. Yet, not everyone who inherits these variations develops the disease.

Researchers at Wake Forest Baptist Medical Center are working to find out why.

In a study published in the October issue of the journal *Kidney International*, the research team evaluated children and siblings of African-Americans on dialysis to determine why some develop kidney disease and others don't. These relatives of the dialysis patients are more likely to inherit the variance in the apolipoprotein L1 (APOL1) gene than members of the general population.

APOL1 gene mutations are associated with up to 40 percent of kidney disease in African- Americans who are treated with dialysis or receive a kidney transplant. This genetic association, which was discovered in 2010 by a team of researchers including Barry Freedman, M.D. professor of nephrology at Wake Forest Baptist, is one of the strongest ever detected for a common disease and helps explain the higher rates of non-diabetic kidney disease among African- Americans relative to the general population.

In this study, the researchers screened 786 close relatives from 470

African-American families with a member who had non-diabetic kidney failure and underwent dialysis. Of the relatives screened, 23 percent had two copies of the gene variant, 47 percent had one copy and 30 percent had no copies. In the general African-American population, the corresponding figures are 12, 39 and 49 percent, respectively.

After adjusting for familial relationships, the researchers found that kidney function, blood pressure and protein in the urine were not significantly different among those with two copies of the variant as compared to those with one or no copies. Weak APOL1 associations with kidney disease were observed after adjusting for age, gender, family age at dialysis and ancestry.

Freedman, the lead author of the study, said the researchers had expected to find a far greater effect of the gene on mild kidney disease in the relatives who had two copies of the variant.

"If the gene alone isn't the trigger, then what is?" he said. "Modifying factors or 'second hits', such as viral infections or environmental factors, must be present to cause kidney disease. More research needs to be conducted in order to identify them.

"We can't change someone's genetic makeup, but if we can find out what the 'second hits' are then hopefully we can find ways to block them and protect people from kidney disease."

The researchers also concluded that there may be limited value in broadly screening African-Americans for this gene variant to detect those with mild kidney disease. This recommendation may change when modifiable second hits are identified, Freedman said. In addition, there may be value in screening certain individuals, particularly relatives of African-American patients on dialysis who may want to donate a kidney.

Provided by Wake Forest University Baptist Medical Center