Transcript Details
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APOL1 and Chronic Kidney Disease: New Findings in African Populations

Announcer:
You're listening to *Clinician's Roundtable* on ReachMD. On this episode, Dr. Rasheed Gbadegesin will discuss the genetic risk factors for kidney disease among West African populations. Dr. Gbadegesin is a Professor of Pediatrics in the Division of Nephrology and Director of the Office of Physician-Scientist Development in the Duke University School of Medicine. Dr. Gbadegesin helped lead a study that analyzed the prevalence of the APOL1 gene, which is commonly linked to chronic kidney diseases in West Africa. Let's hear from Dr. Gbadegesin now.

Dr. Gbadegesin:
This is a collaborative study carried out by the H3 Africa Kidney Research Network. The group comprised of investigators from the US, Canada, Nigeria, Ghana, and other African countries. Regarding the study methodology itself, there is a case control component looking at the association of APOL1 variants with chronic kidney disease in Africans. The second component is a cohort study looking at specific types of CKD, such as biopsy-proven glomerular disease, HIV-associated nephropathy, and sickle cell disease-associated nephropathy, among others. The *New England Journal of Medicine* paper focused on the case control study and included some patients recruited for biopsy-proven glomerular diseases.

In terms of major findings, for the first time, we showed that APOL1 high-risk genotype is a major risk factor for chronic kidney disease and FSGS in Africans living in Africa. That's number one. The second point is we showed that the prevalence of APOL1 high-risk genotype is actually very high in Africa, and it varies between populations. The third one is that we showed that in APOL1, one risk variant can actually be predisposed to CKD or FSGS. Prior to our study, what was known was that you need two risk variants in order for you to develop chronic kidney disease.

The major take-home points from our study are that APOL1 high-risk genotype is more prevalent in the West African population. In this study, the prevalence was about 30 percent compared with 15 percent reported for African Americans. In fact, in some subpopulations in West Africa, the prevalence could be up to 50 percent. So imagine a population where almost half is actually carrying a risk factor for chronic kidney disease, and this risk factor is known to be highly penetrant. In other words, the chances that the person will develop chronic kidney disease with this variant is actually very high; in fact, it's higher than most of the things that we know for IgA nephropathy, for example.

The second significant and unexpected finding is the association between one APOL1 risk variant and FSGS and other chronic kidney diseases. Prior to this study, it was thought that one APOL1 risk variant was relatively benign, or at most, an undetermined intermediate risk, so this was a big surprise for us. It's actually one of the major findings of the study.

So one of the discussion points in the paper is that the high prevalence of APOL1 variant is a primary biological driver of the disparity in the severity and prevalence of CKD in people of African ancestry. And screening for the variants in Africa will make a lot of sense as a public health strategy for primary and secondary prevention of chronic kidney disease in Africa. This is especially important because compounds targeting APOL1 are currently in clinical trials. So knowing the prevalence of these highly penetrant genetic risk factors is very, very important to likely set the stage for these clinical trials.

In addition, much more importantly, facilities for kidney replacement therapy, such as dialysis and kidney transplantation, are rudimentary to nonexistent in Africa, making end-stage kidney disease essentially a death sentence for many patients living with CKD in Africa. Therefore, if we can identify a factor that can lead to early detection and putting in place preventive measures, that is going to

slow down the rate of progression of disease and is going to reduce considerably the morbidity and mortality associated with CKD in Africa.

I suspect that for genetic findings, the next step here would be to replicate the single APOL1 association with CKD in different populations in Africa because this is actually a new finding. The second thing would be to explore the gene-gene and the gene-environment interactions that are driving APOL1 chronic kidney disease in Africa, use these findings to set the stage for clinical trials of compounds targeting APOL1 in Africa, and conduct additional studies to define the genetic architecture of CKD in Africa comprehensively.

Announcer:
That was Dr. Rasheed Gbadegesin talking about the genetic risk factors for kidney disease among West African populations. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!