RESEARCH LETTER

APOL1 Genetic Testing in Patients with Recent African Ancestry and Hypertension: A Pilot Study of Attitudes and Perceptions

To The Editor:

The incidence of kidney failure in African Americans is 2-3 times higher than that in White Americans. A portion of the increased kidney risk appears to be because of polymorphisms in the gene encoding apolipoprotein L1 (*APOL1*). The precise mechanism of how *APOL1* risk variants accelerate kidney disease progression is a matter of intense research, and currently there are no known treatments for *APOL1*-related kidney disease. Currently, there are large National Institutes of Health-funded national studies ("APOLLO" and "LETO") underway to help define the role of *APOL1* genotyping in the context of kidney donation and transplantation[1]; However, the role of *APOL1* genotyping in chronic kidney disease (CKD) care remains unclear.[2,3]

To date, few studies have examined patient perspectives and attitudes about testing for *APOL1*.[4–8] Because *APOL1* risk variants have only been detected among individuals of recent African ancestry, it is essential to engage and incorporate patient perspectives and attitudes about *APOL1* genotyping in clinical decision making and formulation of best practices given the impacts of racism on African Americans as well as the mistrust and underrepresentation of African Americans in clinical trials.

In this pilot study, we offered *APOL1* genetic testing and counseling and assessed the attitudes and concerns related to *APOL1* testing and kidney risk management among self-identified African Americans seen in the Hypertension and Nephrology Clinics at 1 Midwestern academic medical center. In the first phase of this ongoing project, we recruited 128 participants who self-identified as African American. Baseline surveys to assess patient attitudes and concerns about *APOL1* genetic testing and kidney risk management were completed before blood samples were drawn and sent to a Clinical Laboratory Improvement Amendments-approved laboratory for *APOL1* genotyping (Item S1, Item S2, Table S1).

Among the cohort, 71 (55%) were women, and the mean age was 57 years. Nearly 40% of participants (n = 51; 39%) reported an annual family income of <$15,000. Obesity was present in 93 (73%) participants. The median CKD Epidemiology Collaboration 2021 equation estimated glomerular filtration rate was 42 mL/min/1.73 m^2 and median urinary albumin-creatinine ratio was 93 mg/g. A mean of 3 antihypertensive medications were used to achieve a mean systolic blood pressure of 146 mm Hg, and 81 (63%) participants were receiving angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy (Table 1).

Overall, nearly all participants (120 [94%]) reported being concerned about kidney disease. When stratified by CKD stages, 36 (94%), 50 (91%), and 34 (97%) participants with estimated glomerular filtration rates of ≥60, 30-59, and <30 mL/min/1.73 m^2, respectively, reported being concerned about kidney disease (Table S2). Most of the participants thought it was a good idea to be tested for genes that may impact kidney disease (120 [94%]) and would want *APOL1* testing for their children (104 [81%]). Only a small portion (21 [16%]) reported that they would be very upset if genetic results showed that they had a high-risk *APOL1* genotype. Survey responses did not differ appreciably when stratified by CKD stages (Table S2). Participants reported that knowledge of high-risk *APOL1* genotype would lead to positive changes in health-related behaviors, including seeking medical advice and dietary and lifestyle modification (Fig 1). Few individuals (n = 2; <2%) reported that they would take no action and only 1 (<1%) would stop taking blood pressure medications if they were found to have high-risk *APOL1* genotypes. Among the participants genotyped to date, 50 (39%) had 0, 56 (44%) had 1, and 22 (17%) had 2 *APOL1* renal-risk variants (high-risk genotypes).

To our knowledge, our study is one of the first and largest to directly solicit attitudes about *APOL1* genotyping from individuals with CKD. In contrast, prior studies have solicited attitudes about *APOL1* from African Americans in hypothetical nonclinical settings,[4,5] among prior kidney transplant donors,[6,7] and from African Americans without CKD.[8] Our findings of support for *APOL1* testing are largely consistent with these prior reports[4–7] but extend to a clinical population receiving general nephrology and hypertension care, in which the impact of *APOL1* is also relevant.

Patients' strong support for *APOL1* testing was first reported in a smaller (N = 26) study that conducted in-depth interviews on related beliefs and attitudes.[9] In that study, participants endorsed that knowledge of *APOL1* risk would not inspire fatalism or decision regret but motivate health-promoting behaviors[9]—a theme that we replicated in a recent clinical trial[8] and in our study. A recent report of 76 interviews, including researchers, clinicians, and African American patients, family, and community members supported the concept of offering genetic testing to patients, although concerns included risks, such as psychological burdens, misunderstanding, and potential stigma and discrimination.[10] These collective observations suggest that even though there are no proven therapies for *APOL1*-related kidney disease, incorporating *APOL1* testing have benefits in educating patients about kidney risk and encouraging positive health changes.

Two different expert panels have offered recommendations about *APOL1* testing in clinical settings.[2,3] However, these panels disagree in their recommendations about *APOL1* testing in nontransplant settings, with one earlier panel "recommending against the routine offer of *APOL1* testing in clinical care"[2] and a more

Table 1. Participant Characteristics, by CKD Stage.

Characteristics	Overall	Stages 1-2 (eGFR ≥60)	Stage 3 (eGFR 30-59)	Stages 4-5 (eGFR <30)
African American race, n	**128**	**38**	**55**	**35**
Age, y, mean (SD)	57 (13)	50 (11)	60 (11)	61 (13)
Sex, n (%)				
Women	71 (55)	19 (50)	30 (55)	22 (63)
Men	57 (44)	19 (50)	25 (45)	13 (37)
Educational attainment, n (%)				
High school graduate or greater	101 (79)	30 (79)	43 (78)	28 (80)
Less than high school	24 (19)	6 (16)	12 (22)	6 (17)
Not reported	3 (2)	2 (5)	0	1 (3)
Annual family income, n (%)				
Less than $15,000	51 (40)	21 (55)	18 (33)	12 (34)
15,000-$30,000	18 (14)	4 (11)	11 (20)	3 (9)
$30,000-$45.000	15 (12)	3 (8)	9 (16)	3 (9)
≥ $45,000	22 (17)	6 (16)	8 (15)	8 (23)
Not reported	22 (17)	4 (11)	9 (16)	9 (26)
Self-reported overall health, n (%)				
Good to excellent	48 (38)	18 (47)	19 (35)	11 (31)
Fair	59 (46)	15 (39)	25 (45)	19 (54)
Poor to very poor	21 (16)	5 (13)	11 (20)	5 (14)
Blood pressure, mm Hg, mean (SD)				
Systolic	146 (22)	150 (26)	142 (17)	148 (24)
Diastolic	84 (14)	89 (14)	82 (14)	82 (15)
Serum creatinine level, mg/dL, median (IQR)	1.5 (1.2-2.2)	1.0 (0.8-1.2)	1.6 (1.4-1.9)	2.9 (2.3-4.4)
eGFR, mL/min/1.73 m^2, median (IQR)	42 (29-63)	76 (66-90)	42 (37-50)	20 (13-26)
Urinary albumin-to-creatinine ratio, mg/g, median (IQR)[a]	93 (11-634)	52 (8-403)	31 (8-163)	644 (125-1240)
Total cholesterol, mg/dL, mean (SD)[b]	166 (50)	170 (57)	170 (52)	156 (42)
High density lipoprotein cholesterol, mg/dL, mean (SD)[b]	49 (16)	47 (13)	49 (19)	48 (14)
Low density lipoprotein cholesterol, mg/dL, mean (SD)[c]	99 (33)	103 (35)	103 (37)	89 (26)
Triglycerides, mg/dL, mean (SD)[c]	135 (94)	141 (78)	130 (113)	137 (79)
Fasting blood glucose, mg/dL, mean (SD)	113 (55)	109 (49)	118 (56)	108 (60)
Body mass index level, n (%)				
Underweight (<18.5 kg/m^2)	1 (1)	0	0	1 (3)
Normal (18.5 to <25.0 kg/m^2)	17 (13)	6 (16)	6 (11)	5 (14)
Overweight (25.0 to <30.0 kg/m^2)	17 (13)	5 (13)	7 (13)	5 (14)
Obese (≥30.0 kg/m^2)	93 (73)	27 (71)	42 (76)	24 (69)
Antihypertensive agent use, n (%)				
ACEi/ARBs	81 (63)	24 (63)	35 (64)	22 (63)
β-blockers	65 (51)	13 (34)	33 (60)	19 (54)
Calcium channel blockers	84 (66)	21 (55)	38 (69)	25 (71)
Diuretics	65 (51)	17 (45)	29 (53)	19 (54)
Vasodilators	23 (18)	4 (11)	10 (18)	9 (26)
Number of antihypertensive agents, mean (SD)	3 (1)	3 (1)	3 (1)	3 (1)

Note: Percentages reflect column percentages.
Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation.
[a]40% unavailable
[b]28% unavailable
[c]30% unavailable

recent panel recommending that *APOL1* "should be considered in all patients with kidney disease who have African ancestry, particularly when there is a family history of CKD."[3] Our findings suggest that testing was well received by patients who lend support to consideration in clinical practice.

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Although we did not assess health care providers' attitudes about the *APOL1* testing, identifying *APOL1* risk status

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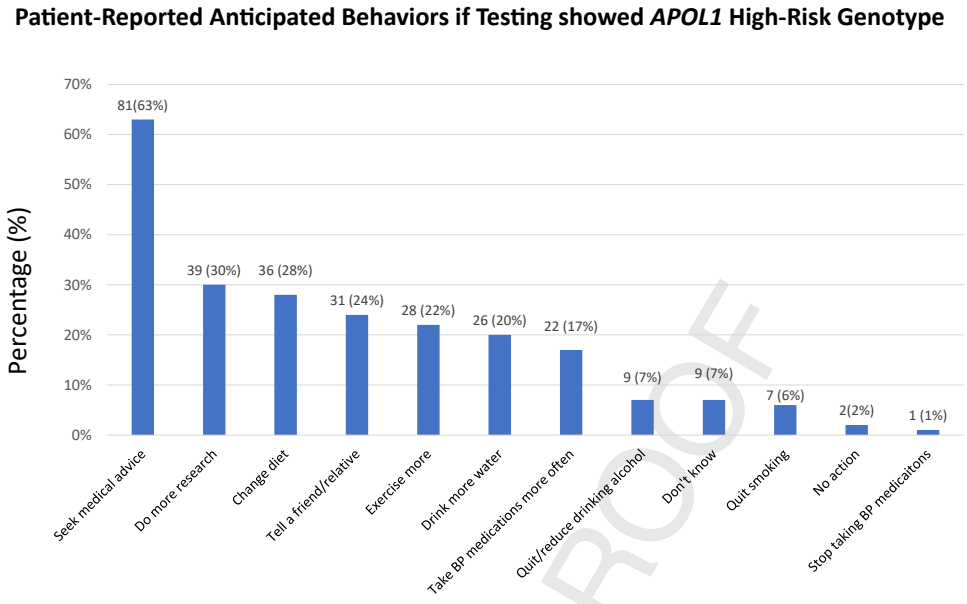

Figure 1. Patient-reported anticipated behaviors if testing showed *APOL1* high-risk genotype. Abbreviation: BP, blood pressure.

in patients with CKD may guide clinicians in monitoring and managing patients at risk of rapid progression. Strict blood pressure control may have a mortality benefit in patients with CKD with high-risk *APOL1* genotypes,[11] and a recent randomized clinical trial showed that disclosing *APOL1* results to clinicians and patients was associated with improved blood pressure control and kidney disease screening.[8] In addition, knowledge of *APOL1* status can motivate clinicians to refer patients for ongoing *APOL1* clinical trials.[12]

Our study has limitations. Findings from 1 center may not be generalized to other populations and practice settings. Patients who agreed to participate may differ from the broader population (eg, they may be more interested in their own health), which may contribute to selection bias. The proportion of high-risk genotypes (17%) was slightly higher than prior general population estimates of ~13%, which likely reflects sampling from nephrology clinics. In addition, although we found that participants may be motivated to engage in health-promoting behaviors after genotyping, the current design did not measure the impact of *APOL1* testing on patient outcomes. However, a recent trial demonstrated improved blood pressure control,[8] and we intend to create a prospective cohort to provide insights on this topic over time.

In conclusion, we report that African American patients at an urban Midwestern medical center were receptive toward *APOL1* genetic testing and believed that testing would motivate changes in health-related behavior. Further research is necessary to determine the optimal patient-centered use of this emerging risk-assessment tool.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Item S1: Additional References

Item S2: Detailed Methods

Table S1: Selected Survey Items

Table S2: Survey Responses Stratified by CKD Stage

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