Do you have patients of African ancestry with CKD?

Consider APOL1-mediated kidney disease (AMKD), a rapidly progressive genetic form of proteinuric kidney disease.[1-3] Those with AMKD progress to dialysis 9 to 12 years earlier than those without AMKD.[2,4]

LEARN MORE INSIDE

UNDERSTANDING AMKD

AMKD is a genetic disease occurring in people of African ancestry with 2 variants of the *APOL1* gene and a second hit, commonly an infection or inflammation.[3,5,6] The presence of 2 *APOL1* risk variants significantly increases the risk of proteinuric kidney diseases, including*:

29X to 89X
HIV-ASSOCIATED NEPHROPATHY[7,8]

17X
FSGS[7]

7X
HYPERTENSION-ATTRIBUTED ESKD[9]

3X to 4X
NONDIABETIC CKD[10]

AMKD is characterized by one or more of the following: proteinuria (ranges from subnephrotic to nephrotic presentation),[1,11] early onset (often age 50 or younger),[7,12] family history of kidney disease,[1] and/or hypertension.[1]

DIAGNOSING AMKD

A definitive diagnosis of AMKD requires a genetic test for the presence of 2 *APOL1* risk variants.[1,11,13,14]

There are diagnostic companies that administer single-gene[15] or panel tests for *APOL1*[16] and provide genetic counseling to help inform care for your patients. An AMKD diagnosis can reassure patients that they are not to blame for their disease.[1] While there are currently no approved treatment options for AMKD, a diagnosis can help better inform patient management by:

- ☑ PROVIDING A CLEARER PROGNOSIS
- ☑ GUIDING TREATMENT DECISIONS
- ☑ OPENING UP CLINICAL TRIAL OPTIONS
- ☑ EMPOWERING PATIENTS WITH KNOWLEDGE

CLINICAL PRESENTATION

AMKD clinical presentations can range from nephrotic FSGS with edema to asymptomatic hypertension-attributed kidney disease with subnephrotic proteinuria.[1,3,11,17] In people of African ancestry, a significant proportion of kidney disease diagnoses are in fact AMKD. In African Americans, AMKD accounts for approximately:

54% to 73% of FSGS[7,9,12,18,19]

62% to 72% of HIV-associated nephropathy[20,21]

23% of hypertension-attributed CKD,[22]
47% of hypertension-attributed ESKD[9]

39% of nondiabetic ESKD[4]

14% of membranous nephropathy[23]

CKD: chronic kidney disease, ESKD: end-stage kidney disease, FSGS: focal segmental glomerulosclerosis
*Some odds ratios have been rounded. See referenced literature for more detailed ranges.

AFRICAN ANCESTRY AND CKD?

THINK AMKD

VISIT APOL1CKD.COM TO DIVE DEEPER INTO THE *APOL1* GENE AND AMKD.

References: 1. Freedman BI, Burke W, Divers J, et al. Diagnosis, education, and care of patients with *APOL1*-associated nephropathy: a Delphi consensus and systematic review. *J Am Soc Nephrol*. 2021;32(7):1765-1778. doi:10.1681/ASN.2020101399 **2.** Elliott MD, Marasa M, Cocchi E, et al. Clinical and genetic characteristics of CKD patients with high-risk *APOL1* genotypes. *J Am Soc Nephrol*. 2023;34(5):909-919. doi:10.1681/ASN.0000000000000094 **3.** Friedman DJ, Pollak MR. *APOL1* and kidney disease: from genetics to biology. *Annu Rev Physiol*. 2020;82:323-342. doi:10.1146/annurev-physiol-021119-034345 **4.** Tzur S, Rosset S, Skorecki K, Wasser WG. *APOL1* allelic variants are associated with lower age of dialysis initiation and thereby increased dialysis vintage in African and Hispanic Americans with non-diabetic end-stage kidney disease. *Nephrol Dial Transplant*. 2012;27(4):1498-1505. doi:10.1093/ndt/gfr796 **5.** May RM, Cassol C, Hannoudi A, et al. A multi-center retrospective cohort study defines the spectrum of kidney pathology in Coronavirus 2019 Disease (COVID-19). *Kidney Int*. 2021;100(6):1303-1315. doi:10.1016/j.kint.2021.07.015 **6.** Nichols B, Jog P, Lee JH, et al. Innate immunity pathways regulate the nephropathy gene Apolipoprotein L1. *Kidney Int*. 2015;87(2):332-342. doi:10.1038/ki.2014.270 **7.** Kopp JB, Nelson GW, Sampath K, et al. *APOL1* genetic variants in focal segmental glomerulosclerosis and HIV-associated nephropathy. *J Am Soc Nephrol*. 2011;22(11):2129-2137. doi:10.1681/ASN.2011040388 **8.** Kasembeli AN, Duarte R, Ramsay M, et al. *APOL1* risk variants are strongly associated with HIV-associated nephropathy in black South Africans. *J Am Soc Nephrol*. 2015;26(11):2882-2890. doi:10.1681/ASN.2014050469 **9.** Genovese G, Friedman DJ, Ross MD, et al. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. *Science*. 2010;329(5993):841-845. doi:10.1126/science.1193032 **10.** Friedman DJ, Pollak MR. APOL1 nephropathy: from genetics to clinical applications. *Clin J Am Soc Nephrol*. 2021;16(2):294-303. doi.10.2215/CJN.15161219 **11.** Rosenberg AZ, Kopp JB. Focal segmental glomerulosclerosis. *Clin J Am Soc Nephrol*. 2017;12(3):502-517. doi:10.2215/CJN.05960616 **12.** Anyaegbu EI, Shaw AS, Hruska KA, Jain S. Clinical phenotype of *APOL1* nephropathy in young relatives of patients with end-stage renal disease. *Pediatr Nephrol*. 2015;30(6):983-989. doi:10.1007/s00467-014-3031-0 **13.** Freedman BI, Kopp JB, Sampson MG, Susztak K. APOL1 at ten years: progress and next steps. *Kidney Int*. 2021;99(6):1296-1302. doi:10.1016/j.kint.2021.03.013 **14.** Peralta CA, Bibbins-Domingo K, Vittinghoff E, et al. *APOL1* genotype and race differences in incident albuminuria and renal function decline. *J Am Soc Nephrol*. 2016;27(3):887-893. doi:10.1681/ASN.2015020124 **15.** Franceschini N, Frick A, Kopp JB. Genetic testing in clinical settings. *Am J Kidney Dis*. 2018;72(4):569-581. doi:10.1053/j.ajkd.2018.02.351 **16.** Thomas CP, Mansilla MA, Sompallae R, et al. Screening of living kidney donors for genetic diseases using a comprehensive genetic testing strategy. *Am J Transplant*. 2017;17(2):401-410. doi:10.1111/ajt.13970 **17.** U.S. Preventive Services Task Force. Screening for chronic kidney disease: recommendation statement. *Am Fam Physician*. 2014;89(4):290A-290B. Accessed February 23, 2024. https://www.aafp.org/pubs/afp/issues/2014/0215/od1.html **18.** Groopman EE, Marasa M, Cameron-Christie S, et al. Diagnostic utility of exome sequencing for kidney disease. *N Engl J Med*. 2019;380(2):142-151. doi:10.1056/NEJMoa1806891 **19.** Kopp JB, Winkler CA, Zhao X, et al. Clinical features and histology of apolipoprotein L1-associated nephropathy in the FSGS clinical trial. *J Am Soc Nephrol*. 2015;26(6):1443-1448. doi:10.1681/ASN.2013111242 **20.** Atta MG, Estrella MM, Kuperman M, et al. HIV-associated nephropathy patients with and without apolipoprotein L1 gene variants have similar clinical and pathological characteristics. *Kidney Int*. 2012;82(3):338-343. doi:10.1038/ki.2012.111 **21.** Kopp JB, Heymann J, Winkler CA. APOL1 renal risk variants: fertile soil for HIV-associated nephropathy. *Semin Nephrol*. 2017;37(6):514-519. doi:10.1016/j.semnephrol.2017.07.004 **22.** Parsa A, Kao WHL, Xie D, et al. *APOL1* risk variants, race, and progression of chronic kidney disease. *N Engl J Med*. 2013;369(23):2183-2196. doi:10.1056/NEJMoa1310345 **23.** Chen DP, Henderson CD, Anguiano J, et al. Kidney disease progression in membranous nephropathy among black participants with high-risk *APOL1* genotype. *Clin J Am Soc Nephrol*. 2023;18(3):337. doi:10.2215/CJN.0000000000000070

VERTEX