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Racial differences in chronic kidney disease incidence and progression among individuals with HIV

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SUMMARY

This Practice Point commentary discusses the findings of Lucas *et al.*'s longitudinal cohort study of chronic kidney disease (CKD) in African American and white individuals with HIV. The study found that—compared with whites—African Americans had a slightly increased risk of incident CKD, but markedly increased rates of estimated glomerular filtration rate decline and progression to end-stage renal disease. This commentary details the clinical implications and limitations of these findings in the context of known racial differences in CKD prevalence and progression to end-stage renal disease in the general population and highlights the importance of screening high-risk HIV patients for kidney disease. CKD is common among HIV patients, and—as in the general population—has a more-aggressive course among African Americans than whites.

Keywords

chronic kidney disease; end-stage renal disease; HIV; racial differences; screening

COMMENTARY

The risk of end-stage renal disease (ESRD) is 3.7 times higher in African Americans than in whites.¹ HIV is a risk factor for ESRD, especially among African Americans, who account for the overwhelming majority (~90%) of cases of ESRD attributable to HIV-associated nephropathy (HIVAN), and in whom HIVAN represents the fourth leading cause of ESRD.¹ In addition, chronic kidney disease (CKD) has been associated with an increased risk of death among individuals infected with HIV.² One study of US Veterans Affairs patients found that the prevalence of advanced CKD (stages 4 and 5) was greater among those with HIV than among those with diabetes (18% vs 13%).³ Furthermore, when analyses were stratified by race, HIV was more strongly associated with ESRD than diabetes among African Americans; however, among whites, HIV was not significantly associated with an increased risk of ESRD. The Veterans Affairs study also found that the rate of estimated glomerular filtration rate (eGFR) decline was greater among African Americans with HIV than among whites with HIV. These findings suggest that there is an important interaction between race and HIV infection on the development of ESRD in HIV-infected persons. Little is known, however, about incident CKD in this population.

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Competing interests

The authors declared no competing interests.

A recent study by Lucas *et al.*⁴ is the first longitudinal cohort study to examine both incident CKD and ESRD in HIV-infected persons. The study analyzed data from 4,259 individuals who were part of the Johns Hopkins HIV Clinical Cohort and had received primary care in the clinic from 1990 onwards. The findings were similar to those of the Veterans Affairs study,³ in that the racial differences were found to be primarily a result of more rapid progression to ESRD rather than due to differences in CKD prevalence and incidence. Only three (10%) white individuals in the study had CKD at baseline (defined as at least two eGFR values <60 ml/min/1.73 m² that were separated by at least 3 months, with more than 50% of follow-up eGFR values <60 ml/min/1.73 m²) compared with 71 (28%) African Americans. At the time of diagnosis of prevalent CKD, African Americans had significantly lower CD4 cell counts, were less likely to have received highly active antiretroviral therapy (HAART), had higher serum creatinine values, greater urinary protein excretion, and lower serum albumin and hemoglobin levels, than whites.⁴

Multivariate analysis of incident CKD in this cohort of patients with HIV showed that African Americans without CKD at enrollment were 1.65 times more likely to develop CKD than whites ($P = 0.048$). Overall, presence of AIDS was the strongest risk factor for incident CKD. Among individuals with either prevalent or incident CKD, robust racial differences in the progression to ESRD were found, with African Americans having an approximately 18 times higher risk of progression to ESRD than whites, which is considerably more than the five times greater risk among African Americans (vs whites) in the general population.⁵ Together with race, other factors significantly associated with progression to ESRD among HIV-infected individuals with CKD included age of 40 years or younger (vs >40 years), increased proteinuria, and non-use of angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers.⁴ Compared with whites with CKD, African Americans with CKD were more likely to have high-grade protein-uria and had a greater than sixfold more-rapid decline in eGFR. Unfortunately, Lucas *et al.* were unable to perform multivariable analysis of factors associated with progression to ESRD because only a single white patient progressed.⁴

The Johns Hopkins HIV Clinical Cohort study also evaluated histopathological findings in a subset of patients with CKD who had undergone kidney biopsy ($n = 73$; 5 whites and 68 African Americans). Consistent with previous literature, HIVAN was found exclusively in African American patients (27 of the 68 who underwent biopsy); however, non-HIVAN pathology was present in the majority (58%) of the 65 patients in whom a diagnosis could be made from biopsy.⁴

In determining the clinical implications of the work by Lucas *et al.*, several points should be considered. Firstly, CKD was defined only by eGFR, which probably resulted in the exclusion of some patients who had proteinuria but preserved renal function. Secondly, ESRD was diagnosed on the basis of initiation of dialysis, and it is unclear how this information was collected and validated; therefore, under-reporting of ESRD may have occurred. Thirdly, and most importantly, there may have been competing risks associated with the development of CKD or ESRD. For example, white individuals in the study may have been more likely to die of HIV-related complications than to progress to ESRD.

Nonetheless, the findings of Lucas *et al.* have important implications. The incidence of ESRD among patients with HIV has decreased, but prevalence is increasing,¹ probably because of improved survival in the HAART era. Since African Americans make up the majority of new HIV cases in the US⁶ and have been shown to be at markedly increased risk of developing ESRD, they represent an important demographic group on which to focus CKD screening and prevention efforts. The finding that African Americans with CKD in the Johns Hopkins study were more likely than whites to have high-grade proteinuria suggests that early screening by assessment of the urinary protein:creatinine ratio could be of benefit in this high-risk group.

Additionally, the use of angiotensin-converting-enzyme inhibitors and angiotensin II receptor blockers was associated with slower progression to ESRD, which makes a case for the use of these medications in HIV-infected patients with proteinuria. Early intervention in individuals known to be at disproportionately increased risk could result in improved outcomes. Further investigation of CKD screening and prevention among high-risk patients with HIV, including the role of HAART, is warranted.

PRACTICE POINT

Racial differences in chronic kidney disease in HIV-infected individuals are largely a result of the markedly increased rates of kidney disease progression among African Americans, making them a very important target population for screening and intervention efforts.

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