Disparities in Identification of CKD

By Moro Salifu, Girish Nadkarni, Steven Coca, and Susanne B. Nicholas

Population-based screening and identification strategies for patients with CKD remain a challenge. Data from the Behavioral Risk Factors Surveillance System suggest that most patients with CKD do not know they have the condition. Screening strategies such as albuminuria and serum creatinine determinations are not widely used in the general population and are performed only on indication; hence, most patients with CKD go undetected, for several reasons.

First, although screening is indicated in patients with traditional risk factors for CKD, including diabetes, hypertension, older age, cardiovascular disease, history of acute kidney injury and a family history of CKD, screening is generally not recommended in patients without risk factors (1). In comparison with whites (71%), the adjusted prevalence of diabetes is 12.6% in African Americans, 16.1% in Native Americans and Alaskan Natives, and 11.8% in Hispanics (2); therefore, minority populations should be targeted for CKD screening.

The prevalence of hypertension among non-Hispanic blacks (41.2%) is higher than that for non-Hispanic whites (28.0%) and Hispanic adults (25.9%); therefore, blacks/African Americans with a history of hypertension should specifically be targeted for CKD screening (3). Furthermore, hypertension awareness (85.7% vs. 82.7%) and treatment rates (77.4% vs. 76.7%) are higher, but hypertension control (49.5% vs. 53.9%) is lower in non-Hispanic blacks than in non-Hispanic whites, suggesting a higher risk for CKD in non-Hispanic blacks (4). Interestingly, these lower rates of blood pressure control are highly prevalent in non-Hispanic blacks, even with higher overall use of blood pressure-lowering medications, further highlighting the need to focus on increasing identification of CKD in particular racial and ethnic groups.

A second consideration regarding disparities in identification of CKD is that compared with individuals of European descent, African Americans have a threefold to fivefold greater risk of CKD, attributed in part to two African ancestral genetic variants (termed G1 and G2) of the APOL1 gene on chromosome 22. Those with two risk alleles have been shown to have a sevenfold to 30-fold increased risk for the development of hypertension-related CKD and faster progression of CKD (5). It is estimated that approximately 36% of African Americans carry at least one APOL1 G1 or G2 risk allele, and 14% carry two APOL1 risk alleles (6). By contrast, G1 and G2 alleles are absent in people of European ancestry. The high allele frequency in the African American population has been attributed to evolutionary selection for their protective effect against infection by the parasitic trypanosome Trypanosoma brucei rhodesiense, which causes the most deadly form of African sleeping sickness. Despite this knowledge, no routine screening test is available for these genetic variants as part of risk stratification for CKD in African American patients with hypertension.

Third, CKD is not part of any incentive-based payment model for primary care physicians (PCPs), and despite the benefits of early referral from primary care to nephrologists (7-9), PCPs may not recognize or recommend specialist care for progressive CKD less frequently than might be expected. The barriers identified for this discrepancy include lack of awareness of clinical practice guidelines and lack of clinical and administrative resources (10, 11).

There is an opportunity to define ways by which PCPs, through incentive-based payments, can have the needed administrative and clinical resources to enhance early referral of patients with CKD. Midlevel providers such as advanced practice nurses can enhance the ability of PCPs to be more efficient at detecting and referring patients early in their CKD trajectory (12). More of such midlevel resources are needed because even when the referral from a PCP to a nephrologist is optimal, we do not have sufficient numbers of nephrologists to manage the volume of referrals.

In the past decade, the number of internal medicine residents choosing nephrology for subspecialty training has progressively declined (13), worsening the already existing and growing shortage of nephrologists. Thus, there is a call to action for guidelines to better define comanagement strategies between PCPs and nephrologists (14). It is conceivable that such comanagement pathways may allow PCPs to provide evidence-based management to patients with CKD stages 1 to 3 (15), while reserving the treatment of patients with CKD stages 4 to 5 for nephrologists and other subspecialists (e.g., endocrinologists, cardiologists, and nutritionists). Shared decision-making has been explored for patients in advanced CKD stages to facilitate their choices for renal replacement therapy (RRT) and end-of-life care but has not been explored at the time of CKD diagnosis (16). Such an approach may likely promote patient engagement in self-care to participate in kidney health strategies.

Taken together, these three considerations constitute a major access issue in CKD. Patients are not identified early, they are not referred early, and there aren’t sufficient numbers of nephrologists to handle the volume of CKD patients in the population. Consequently, minority populations carry the highest burden of delayed referral for CKD care, for a variety of reasons including those related to socioeconomic issues, communication barriers to patient education, and patient-related issues such as patients’ beliefs, religious practices, and lack of trust in the healthcare system.

Physician bias in treating minority patients

Physician bias in treating minority patients also plays a role (17). Even among patients with health insurance, delayed referral to a nephrologist has been shown to be more likely in blacks, Hispanics, and older patients with CKD than in their white or younger counterparts (18, 19).

More recently, Koraishy et al. (20) showed that in a primary care setting, nephrology referrals were significantly more prevalent among patients with fast progression compared with slow progression. Even though a majority of patients with fast progression in the study were not referred, fast progression and being black were associated with increased odds of nephrology referral, suggesting that awareness of the high risk of CKD in black patients can improve the referral rates in this population. Figure 1 shows a model of early versus late referral in CKD. Early referral provides better patient treatment and better access to all forms of renal replacement therapy (RRT). Late referral results in worse outcomes and in most patients having undergone hemodialysis before they have access to peritoneal dialysis or transplantation as their choice of RRT.

Recent advances in informatics, data science, and molecular biomarkers may be a potential solution to these problems. Electronic medical records have been adopted nearly universally across health systems, and although they have certain limitations, they contain a multitude of longitudinal granular information. This information can be integrated with prognostic biomarkers that have high predictive value in early CKD (21) and genomic information (such as APOL1 genotyping) (22) with the use of advanced data science techniques. Thus, comprehensive, multidimensional assessments of kidney risk in high-risk individuals (especially those with type 2 diabetes and those of African ancestry) can be generated and integrated with both the electronic medical record and care management tools, ensuring that appropriate care guidelines are being followed and tracked.

Finally, large-scale analytics can be performed to quantify the population health impact of these measures, especially in vulnerable minority populations.
Disparities in Risk Factors for Progression of CKD

By Moro Salifu and Susanne B. Nicholas

Many patients with CKD invariably experience progression, slow or fast, to later CKD stages and require renal replacement therapy at some point. Controlling the primary risk factors for CKD has been shown to slow progression of CKD but does not prevent the development of ESRD. The mechanisms underlying slow or fast progression of CKD are complex but are generally attributable to nephron loss from the primary disease, which sets a vicious circle of worsening renal function. The processes are particularly described in diabetic nephropathy, in which podocyte loss may be a downstream effect (4).

The glomerulus is the site of the renin-angiotensin aldosterone system, development of metabolic acidosis, and, to a lesser extent, dyslipidemia and anemia further contribute to a progressive decline in renal function (5), although the rate of progression is slower in African Americans than in other racial and ethnic groups. Additional factors, such as the renin-angiotensin aldosterone system, BP, and response to injury, have been described to demonstrate marked racial disparities in physiology and in response to treatment (6).

African Americans demonstrate lower plasma renin levels than do other racial groups (7, 8), which suggests that non-renin-mediated mechanisms play a major role in the pathogenesis of hypertension in this population. African Americans are more salt sensitive than are other racial groups (5), which results in greater amounts of salt and water retention, ultimately leading to plasma volume expansion and hypertension. This picture is further exacerbated by sympathetic overdrive in African Americans, largely resulting from socioeconomic stressors, which further drive hypertension (9).

Response to injury is also exacerbated in African Americans, as evidenced by overexpression of TGF-β1 in patients with hypertension and kidney disease (10). TGF-β induces fibrosis during the repair of tissue injury and is a major mediator of glomerulosclerosis (11). It is also postulated that TGF-β1 modulates the expression of angiotensin receptor II (12) and endothelin (13), further resulting in ischemia and injury to tissues. Taken together, TGF-β1 is overly expressed in African American patients with CKD and contributes to the progression of CKD in this patient population.

Differences in other risk factors for CKD and for CKD progression play important roles in the disparities associated with CKD. These risk factors may be divided into traditional and nontraditional risk factors. The traditional risk factors, such as diabetes, hypertension, history of acute kidney injury, malignancy, advancing age, cardiovascular disease, obesity, metabolic syndrome, and long-term use of nephrotoxic agents such as nonsteroidal inflammatory drugs, are all well known and may be influential in all individuals.

Nontraditional risk factors, such as poverty, lack of access to optimal healthcare, lack of health insurance, environmental factors, cultural belief, language and literacy barriers, and genetics, also described as social determinants of health, have been shown to play a greater role in ethnic minorities (14). In several instances, social conditions may have a direct effect on kidney disease and kidney disease progression. For example, it has been shown that reduced annual household income is associated with greater odds of both microalbuminuria and macroalbuminuria (15). Further, uninsured compared with insured individuals may be less likely to receive clinical care for optimal BP control (16), which may have a direct impact in CKD progression, particularly in African Americans.

Indeed, African Americans are susceptible to CKD progression not only from molecular and environmental factors but also from genetic factors. In one prospective study, Salifu et al. (17) showed that between African Americans and whites under equivalent glycemic control, there was no significant difference in diabetic CKD progression from one stage to the next, which suggests that other factors may explain the previously observed differences. APOL1 high-risk variants are associated with greater risk of incident proteinuria and CKD in African Americans (18). In fact, the APOL1 risk variants and interplay with environmental factors may account for up to 70% of the differences in the prevalence of kidney failure in African Americans compared with whites and individuals with nonendemic kidney disease (19).

References