Race and Kidney Disease Outcomes: Genes or Environment?

Sylvia Ramirez

University Renal Research and Education Association (URREA), Ann Arbor, Michigan

Editorial

The fundamental question that must be answered to address racial/ethnic differences in renal disease care and outcomes begins by defining (1) the degree to which these differences can be accounted for by disparities in access to and quality of care and (2) the extent to which these differences can be attributed to biologic or physiologic differences. Identifying these components is essential because the former can only be addressed by changes at the health systems level, whereas the latter would require clinical interventions at the patient level. To elucidate racial/ethnic differences in access to care, the National Healthcare Quality and Disparities Reports, by performing extensive analysis of data from over 40 established national databases, have revealed the following key findings: (1) Currently, the US health care system does not consistently provide high quality care; (2) health care quality for approximately 140 quality measures and 100 access measures is particularly problematic in racial/ethnic and socioeconomic subgroups; (3) disparities are especially pronounced in providing preventive care; (4) improvement in these disparities is possible (1).

For kidney disease, in particular, there is an extensive body of literature that documents the disproportionate burden of disease, as well as the access to and quality of care for the largest minority groups in the United States compared with the white population. For instance, although quality improvement efforts in hemodialysis care in the United States have demonstrated a marked improvement in the proportion of African-American patients who have achieved certain target indicators for dialysis care, particularly dialysis dose and anemia management, gaps in the achievement of these indicators between African Americans and whites persist, and in some geographic regions have increased even further (2). Disparities are particularly evident in access to renal transplantation as shown in the Dialysis Outcomes and Practice Patterns Study (DOPPS), in which African-American patients were significantly less likely to be placed on the transplant waiting list as compared with white patients (3). In elucidating the basis for these differences in access to the transplant waiting list, African Americans were less likely to be rated as appropriate candidates for transplantation based on clinical opinion and were less likely to complete transplant evaluation (4). The differences in quality of care persist even at transplantation. In a retrospective cohort study of all deceased-donor adult recipients in the United States from 1996 to 2002, African Americans and Asians had a greater likelihood of receiving lower quality organs relative to white recipients (5). The reduced transplantation rate among minorities is partially attributed to lower rates of HLA matching, and although the number of deceased-donor kidney transplants performed among minority populations has increased because of the recent elimination of matching points for HLA-B antigen, the gap in transplantation across racial groups still persists (6).

In addition to identifying variations in access and quality of care, it is equally important to determine the extent to which improving access to care can improve clinical outcomes. Recent clinical studies argue that strong biologic forces may override the impact of access or quality of care in certain conditions. For instance, despite having no statistically significant differences in BP management, glycemic control, use of angiotensin-converting enzyme (ACE) inhibitors, and baseline proteinuria, Indo-Asians (Indians, Pakistanis, and related ethnic populations) were found to have significantly accelerated rates of decline in renal function compared with whites (7). Similarly, in the Pathways Study, an epidemiologic study of depression in a population-based sample of diabetic patients in Washington state, African Americans, Asians, and Hispanics were more likely than whites to have microalbuminuria and macroalbuminuria, depending on the presence or absence of concomitant hypertension. These differences were observed even after adjusting for diabetes care characteristics, diabetes duration, and other clinical factors (8).

In this issue of JASN, two studies enhance our understanding of how race or ethnicity influences access to care and clinical outcomes. Tillin et al., in population-based studies done in London, sought to identify whether race modifies the association between microalbuminuria and cardiovascular disease, hypothesizing that African Caribbeans and Southeast Asians from India, Pakistan, and Bangladesh, given the higher rates of hypertension in the former and cardiovascular disease in the latter, would have higher rates of microalbuminuria (9). Using timed, overnight urine collections to measure the albumin excretion rate, the authors found racial differences in the prevalence of microalbuminuria, as well as a modification by race of the relationship between microalbuminuria and prevalent cardiovascular disease. African-Caribbean men and women were found to have the highest prevalence of microalbuminuria, whereas Southeast Asian men were found to have the lowest prevalence. In addition, there was a strong association between
microalbuminuria and cardiovascular disease, as well as with cardiac mortality, among Southeast Asians (men), whereas microalbuminuria was inversely associated with cardiovascular disease among African Caribbeans. However, none of these remained significant after adjusting for age, smoking status, glucose tolerance category (including presence of diabetes), and systolic BP. This suggests that the observed differences are largely explained by these adjustment factors. With these findings, the authors propose that different mechanisms are responsible for microalbuminuria and its association with cardiovascular disease in different racial groups. For Southeast Asians, the authors invoke the possibility of insulin resistance or the metabolic syndrome to account for the association, whereas for African Caribbeans, the authors cite better lipid profile as a protection from concomitant microalbuminuria and cardiac disease, attributing microalbuminuria instead to other undiagnosed glomerulopathies.

Although Tillin et al. suggested potential differences in mechanisms for microalbuminuria and its relationship with cardiovascular disease, the study had several limitations that need to be considered. First, there was a high dropout rate because of failure to collect urine specimens for calculation of albumin excretion rate (27% overall). This was significantly different across racial groups, with close to one third of Southeast Asians (both men and women) having missing albumin excretion rates. This differential dropout rate across racial groups may introduce a selection bias. Indeed, this raises the limitation of relying on a timed urine collection for defining microalbuminuria. As the Kidney Disease Outcomes Quality Initiative (K/DOQI) guideline suggests, a spot urine albumin:creatinine ratio is less fraught with error because of concern for incompleteness in urine collection (10). This paper calls for more detailed study of racial differences in proteinuria and the race-specific risk factors.

Examining a different aspect of racial disparities in care, Hall and colleagues investigated differences in rates of renal transplantation and mortality among other, less-studied minority populations, namely Asians and Pacific Islanders (11). In this study of 24,963 adults from Network 17 (Transpacific Renal Network), the authors found significantly lower mortality rates across certain Asian and Pacific Islander dialysis populations, in particular the Japanese, Chinese, Filipinos, Samoans, as well as the Asians and Pacific Islanders residing in Northern California. Geographic differences in outcomes were also identified, particularly in pre-ESRD care, where it was noted that Asians and Pacific Islanders living outside Hawaii and the Pacific Islands initiated dialysis with significantly lower serum albumin and significantly higher serum creatinine and blood urea nitrogen (BUN) levels compared with those living in Northern California. A most striking finding in support of geographic influence is that Pacific Islanders (Chamorrans) who resided in their native region had the highest adjusted mortality rate, whereas Asians and Pacific Islanders from Northern California were found to have the lowest adjusted mortality rate. This suggests that given similar genetic make-up, care received in different geographic regions can result in highly disparate clinical outcomes.

Consistent with previous investigations, all the minority groups studied were also determined to have significantly lower transplantation rates, regardless of geographic location. Particularly disadvantaged were Hawaiians, Samoans, and Chamorrans residing in their home islands. Altogether, this study demonstrates the marked disparities in pre-ESRD care and access to transplantation received by Asians and Pacific Islanders residing outside of the mainland United States. This is in contrast to the improved care among US Asians as revealed by the Centers for Medicare and Medicaid Services (CMS) Clinical Performance Measures study, in which Asians were determined to have superior intermediate outcomes, including dialysis adequacy, use of an arteriovenous fistula, and serum albumin, compared with whites and African Americans (12).

The two papers in this issue of JASN raise even more questions relating to race as a determinant for outcomes in renal disease. More importantly, to truly address these disparities in quality and access to care, as well as in patient outcomes, further study should begin to focus on identifying the mechanisms for these differences, followed by defining effective interventions. Indeed, these two studies, in addition to already existing literature, only emphasize the need for a comprehensive and integrated approach in elucidating the mechanisms for racial/ethnic disparities in clinical care and outcomes.

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