Racial Disparities in Kidney Disease Outcomes

Susanne B. Nicholas, MD, MPH, PhD1,2, Kamyar Kalantar-Zadeh, MD, MPH, PhD3, and Keith C. Norris, MD2

1Division of Nephrology and Division of Endocrinology, Diabetes and Hypertension, David Geffen School of Medicine at University of California, Los Angeles, CA, USA
2Department of Medicine, David Geffen School of Medicine at University of California, Los Angeles and Charles R. Drew University of Medicine and Science, Los Angeles, CA, USA
3Division of Nephrology and Hypertension, University of California Irvine, Orange, CA, USA

Abstract

Chronic kidney disease (CKD) is a national public health problem. While the prevalence of early stages of CKD is similar across different racial/ethnic and socioeconomic groups, the prevalence of end-stage renal disease (ESRD) is greater for minorities than their non-Hispanic white peers. Paradoxically, once on dialysis minorities experience survival rates that exceed their non-Hispanic white peers. Advancing our understanding of the unique interplay of biological, genetic, environmental, socio-cultural, and health care system level factors may prompt reorientation of our approach to health promotion and disease prevention. The potential of this new approach is to create previously unimagined gains to improve patient outcomes and reduce health inequities for patients with CKD.

Keywords

racial disparities; chronic kidney disease

Introduction

Chronic kidney disease (CKD) is a national public health problem1 that has been recognized globally as an important cause of premature morbidity and mortality. Despite similar rates of the early stages of CKD across different racial/ethnic and socioeconomic groups, the prevalence of end-stage renal disease (ESRD) is greater for minorities than their non-Hispanic white peers2,3 (Figure 1). The existence of these disparities in health outcomes provides an opportunity to better understand many of the unique unrecognized biological, genetic, environmental, socio-cultural, and health care system level factors and biases that ultimately can lead to improved clinical outcomes for all CKD patients4-7 (Figure 2). Examples range from the recent advances in genetic underpinnings due to variations in the
APOL gene\textsuperscript{8,9} and the role of inflammation\textsuperscript{10,11}, that may soon lead to novel diagnostic and therapeutic options to tackling socio-cultural influences on CKD\textsuperscript{4-6}. In addition, the promotion of universal forms of health care and/or more structured medical care systems\textsuperscript{7} may be vital prospects to advance our knowledge. These approaches can ensure that \textit{all} persons can receive timely quality care. A new integration of these factors may prompt the renal community to explore new avenues towards health promotion and disease prevention, and hopefully achieve greater improvements in patient outcomes and reduced health inequities.

The objectives of this overview are to provide a background of key CKD risk factors that vary greatly in prevalence by gender or race/ethnicity as well as racial/ethnic disparities in CKD and ESRD mortality risk, and then to investigate in more depth potential mediators and novel interventions to address the CKD epidemic.

**Defining CKD**

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines define CKD as the presence of markers of kidney damage such as albuminuria and/or a sustained reduction (≥3 months) in estimated glomerular filtration rate (eGFR) stratified by five progressive stages of the disease based on falling eGFR\textsuperscript{12}. The guidelines provide specific evaluation and treatment recommendations. The inclusion of the presence of markers of kidney damage such as albuminuria allows for the clinical identification of CKD in its earliest stages when the disease may be asymptomatic and eGFR might still be well within the normal limits. This was a major advance for the nephrology community since if left undiagnosed and untreated, CKD can progress inexorably to ESRD and/or associated complications such as premature cardiovascular disease (CVD)\textsuperscript{11}. The KDOQI and more recent Kidney Disease Improving Global Outcomes (KDIGO) guidelines\textsuperscript{13} support the promotion of targeted patient and population level screening and early interventions to address this global problem\textsuperscript{14}.

**Race/Ethnicity and End-Stage Renal Disease**

Disparities in CKD may be related to many factors such as socio-economic status, gender, race/ethnicity among others\textsuperscript{4-6} (Figure 3). Because of the lack of identification of physiologic or biologic differences that confer the notable added risk for CKD and ESRD to minorities, the findings of such tremendous disparities in ESRD incidence and prevalence was surprising. A seminal paper by Rostand and colleagues\textsuperscript{15} noted an average of a 4-fold higher race-specific risk for developing ESRD among blacks in Jefferson County, Alabama in comparison to their white counterparts. This was highlighted by >17-fold greater rate of hypertension as the ESRD etiology among blacks. This high rate of ESRD occurs despite similar or even lower prevalence rates of early stage CKD\textsuperscript{16}, reinforcing the need to better identify and treat biologic and health care system level factors that may mediate their disproportionate progression to ESRD. The excess rate of ESRD among minorities not only levies a personal toll on affected families and communities, but the excess prevalence of ESRD now accounts for nearly $15 billion (Medicare and non Medicare) a year in ESRD costs.

In spite of the racial disparities in ESRD incidence and prevalence, and the recognition of ESRD quality care indicators\textsuperscript{17-19}, minority patients with advanced CKD on dialysis display a greater adjusted survival rate than their non-Hispanic white colleagues\textsuperscript{10,20,21}. This survival advantage appears to be consistent for Hispanics of all ages and may represent an extension of surprising high survival rates in the general U.S. population despite the high prevalence of many high risk chronic diseases. The survival advantage for black ESRD

\textit{Semin Nephrol.} Author manuscript; available in PMC 2014 September 01.
patients is particularly surprising given the substantially reduced life expectancy for blacks compared with whites in the general population\textsuperscript{22}. The survival advantage among black ESRD patients is driven mainly by survival rates in persons >50 years of age where ESRD-related cardiovascular events are driven by oxidative stress, inflammation, oxidation-prone intermediate-density lipoproteins, high-density lipoprotein deficiency and dysfunction, hypertension, vascular calcification, and arrhythmias\textsuperscript{23,24}. On the other hand, mortality rates among younger African American ESRD patients appear to be similar to or greater than whites, likely driven more by socio-economic and cultural factors\textsuperscript{25}. A better understanding of the factors mediating the survival paradox of the African American and Hispanic dialysis populations might improve outcomes in all patients with CKD as well as other chronic diseases with high rates of premature morbidity and mortality.

**Inflammation and ESRD Outcomes**

A multitude of factors influence ESRD outcomes in African American patients on dialysis (Figure 4) and could be targets to explain unexpected differences in survival. In addition to differences in nutritional status\textsuperscript{10,11}, racial/ethnic differences in inflammation may be a critical contributor. Noori et al. reported a strong association of higher levels of C-reactive protein (CRP) and interleukin-6 (IL-6), but not TNF-\(\alpha\) with increased adjusted mortality risks in 799 African American and white dialysis patients followed over a period of 6 years\textsuperscript{26}. The highest quartile of IL-6 (vs. the lowest) was associated with 2.4 and 4.1 times higher risk of death in African Americans and whites, respectively. Crews and colleagues\textsuperscript{11} supported a significantly lower adjusted mortality rate in African Americans compared with Caucasians (34\% versus 56\%) among 816 incident hemodialysis patients followed for 3 years. The survival advantage of African American dialysis patients was only seen in the presence of the highest levels of CRP and IL-6. By contrast, survival disparities between African American and Caucasian dialysis patients did not exist in the presence of low-level inflammation. Streja and co-workers reported lower mortality rates for blacks and Hispanics than non-Hispanic whites after traditional case-mix adjustment in over 124,000 dialysis patients followed over 5 years\textsuperscript{8}. However, after additional control for nutritional status and inflammation surrogates, Hispanics had mortality similar to non-Hispanic whites, and African Americans had even higher mortality, suggesting that survival advantage of African American and Hispanic hemodialysis patients may be related to differences in nutritional and inflammatory status. Together, these studies suggest that survival advantage of minority hemodialysis patients might be more resilient when confronted with the deleterious effects of inflammation.

**Access to Care**

Overcoming barriers to quality health care is crucial for optimizing health outcomes (Figure 5)\textsuperscript{7}. A single payer system has been proposed as a powerful approach to reducing disparities in access to care, delivery of care and associated health outcomes. Tarver-Carr et al. reported much lower rates of cardiovascular procedures among women and minorities with CKD not on dialysis when coverage was dispersed among multiple providers. However, after the onset of ESRD and transition to Medicare, a single payer system, the rate of cardiovascular procedures was similar for all ESRD patients\textsuperscript{27}. A single payer system has also been associated with racial/ethnic equity for KDOQI CKD recommended targets\textsuperscript{28}. A pooled analysis of four community-based studies where coverage was dispersed among multiple providers, suggested a survival disadvantage (composite end points of death and nonfatal myocardial infarction) for blacks with CKD,\textsuperscript{29} whereas, a survival advantage was noted for blacks with diabetic nephropathy seen at the Veterans Administration, also a single payer system\textsuperscript{30}. In addition to strategies such as a single payer system, an integrated team approach (Figure 6) can help to better coordinate the complicated needs of many patients\textsuperscript{31}.

*Semin Nephrol*. Author manuscript; available in PMC 2014 September 01.
This may be particularly important for patients with multiple health care needs such as those with CKD. An integrated approach can help to coordinate care and improve health care delivery across the existing multiple payer system, leverage a team of health professionals (physicians, nurses, social workers, dietitians, pharmacists) and provide system level support for patient self-monitoring of key co-morbid health conditions such as diabetes and hypertension.

**Health Equity through Action on the Social Determinants of Health**

The persistence of health inequities in the United States is an indictment of the institutionalization of moral apathy and likely contributes to our ranking of last place in preventable deaths among developed nations, despite our recognized standing as the world leader in health technology and medical care. Dr. Steven Schroeder, former president of the Robert Wood Johnson Foundation, presented a compelling case for concentrating strategies on actionable determinants of personal health behavior, social factors, health care, and the environment. He argued that since the less fortunate are disproportionately affected by these actionable determinants of health we must focus on this population to improve the health of the American. This sentiment is mirrored by the World Health Organization which has identified three key tenets to improving health at a global level: 1) Improve the conditions of daily life, 2) Tackle the inequitable distribution of power, money, and resources - the structural drivers of those conditions of daily life - globally, nationally, and locally, and 3) Develop a workforce trained in the social determinants of health, and raise public awareness about the social determinants of health. One example of the influence of inequity and health is that of education. It has been estimated that as many as 30,000 deaths annually could be potentially averted by medical advances, whereas over 200,000 deaths annually could be averted by eliminating education-associated excess mortality. The relationship between education and CKD was highlighted by Choi et al. who examined over 61,000 participants enrolled in the National Kidney Foundation's Kidney Early Evaluation Program (KEEP), a national health screening initiative. Higher educational attainment (college graduates compared to persons not completing high school) was associated with significantly lower adjusted odds of having hypertension, 0.71 (95% confidence interval [CI], 0.66-0.76); diabetes, 0.77 (95% CI, 0.72-0.81); cardiovascular disease, 0.62 (95% CI, 0.57-0.68); current or previous smoking, 0.57 (95% CI, 0.54-0.60); obesity, 0.83 (95% CI, 0.79-0.88); decreased kidney function, 0.89 (95% CI, 0.82-0.96); and albuminuria, 0.72 (95% CI, 0.67-0.78). Importantly, during a mean follow-up of 3.9 years those who had completed college had 24% lower mortality compared with participants who had completed at least some high school (p<0.001) (Figure 7).

**The Way Forward**

At a public health level, continuing efforts to ensure that all Americans have access to and receive quality health care is critical to positively impact the CKD epidemic and particularly the disparities in both CKD and ESRD. Steps to minimize the adverse social determinants of health, to improve provider-patient communication, increase access to evidence-based care and the re-conceptualization of health and health care, including health beliefs and practices and a broader understanding of the interconnection of the mind, body and spirit may herald a new era in U.S. health and new hope for patients with CKD and ESRD.

**Acknowledgments**

**Financial Support:** This work is funded in part by NIH grants U54MD007598 (SBN, KCN), UL1TR000124 (KCN), P30AG021684 (KCN), and P20-MD000182 (KCN), Burnham and Hubrecht Endowment (SBN) and K24-DK091419 and R01-DK078106 (KKZ). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
References

1. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. JAMA. 2007; 298:2038–47. [PubMed: 17986697]
2. Collins AJ, Foley RN, Herzog C, et al. US Renal Data System 2012 Annual Data Report. Am J Kidney Dis. 2013; 61:A7. [PubMed: 23253259]
3. Collins AJ, Foley RN, Herzog C, et al. US Renal Data System 2010 Annual Data Report. Am J Kidney Dis. 2011; 57:A8, e1–526. [PubMed: 21184928]
4. Norris K, Nissenson AR. Race, gender, and socioeconomic disparities in CKD in the United States. J Am Soc Nephrol. 2008; 19:1261–70. [PubMed: 18525000]
5. Norris KC, Agodoa LY. Unraveling the racial disparities associated with kidney disease. Kidney Int. 2005; 68:914–24. [PubMed: 16105022]
6. Powe NR. To have and have not: health and health care disparities in chronic kidney disease. Kidney Int. 2003; 64:763–72. [PubMed: 12846781]
7. Powe NR. Let's get serious about racial and ethnic disparities. J Am Soc Nephrol. 2008; 19:1271–5. [PubMed: 18524999]
8. Freedman BI, Kopp JB, Langefeld CD, et al. The apolipoprotein L1 (APOL1) gene and nondiabetic nephropathy in African Americans. J Am Soc Nephrol. 2010; 21:1422–6. [PubMed: 20688934]
9. Genovese G, Friedman DJ, Ross MD, et al. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. Science. 2010; 329:841–5. [PubMed: 20647424]
10. Streja E, Kovesdy CP, Molnar MZ, et al. Role of nutritional status and inflammation in higher survival of African American and Hispanic hemodialysis patients. Am J Kidney Dis. 2011; 57:883–93. [PubMed: 21239093]
11. Crews DC, Sozio SM, Liu Y, Coresh J, Powe NR. Inflammation and the paradox of racial differences in dialysis survival. J Am Soc Nephrol. 2011; 22:2279–86. [PubMed: 22021717]
12. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002; 39:S1–266. [PubMed: 11904577]
13. Levey AS, Atkins R, Coresh J, et al. Chronic kidney disease as a global public health problem: approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. Kidney Int. 2007; 72:247–59. [PubMed: 17568785]
14. McCullough PA, Steigerwalt S, Tolia K, et al. Cardiovascular disease in chronic kidney disease: data from the Kidney Early Evaluation Program (KEEP). Curr Diab Rep. 2011; 11:47–55. [PubMed: 21076895]
15. Rostand SG, Kirk KA, Rutsky EA, Pate BA. Racial differences in the incidence of treatment for end-stage renal disease. N Engl J Med. 1982; 306:1276–9. [PubMed: 7040967]
16. Hsu CY, Lin F, Vittinghoff E, Shlipak MG. Racial differences in the progression from chronic renal insufficiency to end-stage renal disease in the United States. J Am Soc Nephrol. 2003; 14:2902–7. [PubMed: 14569100]
17. Owen WF Jr, Chertow GM, Lazarus JM, Lowrie EG. Dose of hemodialysis and survival: differences by race and sex. JAMA. 1998; 280:1764–8. [PubMed: 9842952]
18. Hopson S, Frankenfield D, Rocco M, McClellan W. Variability in reasons for hemodialysis catheter use by race, sex, and geography: findings from the ESRD Clinical Performance Measures Project. Am J Kidney Dis. 2008; 52:753–60. [PubMed: 18514986]
19. Reddan D, Klassen P, Frankenfield DL, et al. National profile of practice patterns for hemodialysis vascular access in the United States. J Am Soc Nephrol. 2002; 13:2117–24. [PubMed: 12138144]
20. Kalantar-Zadeh K, Golan E, Shohat T, Streja E, Norris KC, Kopple JD. Survival disparities within American and Israeli dialysis populations: learning from similarities and distinctions across race and ethnicity. Semin Dial. 2010; 23:586–94. [PubMed: 21175833]
21. Kovesdy CP, Anderson JE, Derose SF, Kalantar-Zadeh K. Outcomes associated with race in males with nondialysis-dependent chronic kidney disease. Clin J Am Soc Nephrol. 2009; 4:973–8. [PubMed: 19369403]
22. Davey Smith G, Neaton JD, Wentworth D, Stamler R, Stamler J. Mortality differences between black and white men in the USA: contribution of income and other risk factors among men
screened for the MRFIT. MRFIT Research Group. Multiple Risk Factor Intervention Trial. Lancet. 1998; 351:934–9. [PubMed: 9734939]

23. Vaziri ND, Norris KC. Reasons for the lack of salutary effects of cholesterol-lowering interventions in end-stage renal disease populations. Blood Purif. 2013; 35:31–6. [PubMed: 23343544]

24. Kucirka LM, Grams ME, Lessler J, et al. Association of race and age with survival among patients undergoing dialysis. JAMA. 2011; 306:620–6. [PubMed: 21828325]

25. Kalantar-Zadeh K, Kovesdy CP, Norris KC. Racial survival paradox of dialysis patients: robust and resilient. Am J Kidney Dis. 2012; 60:182–5. [PubMed: 22495468]

26. Noori N, Kovesdy CP, Dukkipati R, et al. Racial and ethnic differences in mortality of hemodialysis patients: role of dietary and nutritional status and inflammation. Am J Nephrol. 2011; 33:157–67. [PubMed: 2193117]

27. Tarver-Carr ME, Powe NR, Eberhardt MS, et al. Excess risk of chronic kidney disease among African-American versus white subjects in the United States: a population-based study of potential explanatory factors. J Am Soc Nephrol. 2002; 13:2363–70. [PubMed: 12191981]

28. Gao SW, Oliver DK, Das N, et al. Assessment of racial disparities in chronic kidney disease stage 3 and 4 care in the department of defense health system. Clin J Am Soc Nephrol. 2008; 3:442–9. [PubMed: 18199843]

29. Weiner DE, Tighiouart H, Amin MG, et al. Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies. J Am Soc Nephrol. 2004; 15:1307–15. [PubMed: 15100371]

30. Young BA, Maynard C, Boyko EJ. Racial differences in diabetic nephropathy, cardiovascular disease, and mortality in a national population of veterans. Diabetes Care. 2003; 26:2392–9. [PubMed: 12882868]

31. Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? Eff Clin Pract. 1998; 1:2–4. [PubMed: 10345255]

32. Fahey T, Schroeder K, Ebrahim S. Educational and organisational interventions used to improve the management of hypertension in primary care: a systematic review. Br J Gen Pract. 2005; 55:875–82. [PubMed: 16282005]

33. Nolte E, McKee CM. Measuring the health of nations: updating an earlier analysis. Health Aff (Millwood). 2008; 27:58–71. [PubMed: 18108480]

34. Schroeder SA. Shattuck Lecture. We can do better--improving the health of the American people. N Engl J Med. 2007; 357:1221–8. [PubMed: 17881753]

35. Marmot M, Friel S, Bell R, Houweling TA, Taylor S. Closing the gap in a generation: health equity through action on the social determinants of health. Lancet. 2008; 372:1661–9. [PubMed: 18994664]

36. Woolf SH, Johnson RE, Phillips RL Jr, Philipsen M. Giving everyone the health of the educated: an examination of whether social change would save more lives than medical advances. Am J Public Health. 2007; 97:679–83. [PubMed: 17329654]

37. Choi AI, Weekley CC, Chen SC, et al. Association of educational attainment with chronic disease and mortality: the Kidney Early Evaluation Program (KEEP). Am J Kidney Dis. 2011; 58:228–34. [PubMed: 21601328]

38. Nicholas S, Agodoa L, Norris K. Ethnic disparities in the prevalence and treatment of kidney disease. Nephrol News Issues. 2004; 18:29–30. 2, 4 passim. [PubMed: 15595498]

39. Smedley BD. Moving beyond access: achieving equity in state health care reform. Health Aff (Millwood). 2008; 27:447–55. [PubMed: 18332501]
Figure 1.
Prevalence of CKD and ESRD by Race/Ethnicity. Adapted from^{2,16}.
Figure 2.
Overview of differences, disparities, and discrimination on quality of health care and overall health outcomes\(^4\). Adapted from\(^{59}\)
Figure 3.
A framework for integrating the influence of key socio-cultural determinants of CKD\textsuperscript{4}.
Adapted from\textsuperscript{5}

\textit{Semin Nephrol}. Author manuscript; available in PMC 2014 September 01.
Figure 4.
Key Factors Influencing ESRD Outcomes and the Survival Paradox of African American Dialysis Patients

Semin Nephrol. Author manuscript; available in PMC 2014 September 01.
Figure 5.
Potential Barriers in Access and Quality of Health Care\textsuperscript{7}
Figure 6.
The Chronic Care Model\textsuperscript{4,31}
Figure 7.
Probability of survival by level of educational attainment\textsuperscript{37}
Figure 8.
CKD: A Call to Action. Adapted from 38

Patient-Provider Level
- Risk factor education with targeted early interventions for high-risk individuals
- Increased awareness of cultural differences in primary values, world views
- Effective communication
- Understanding socio-cultural & biologic contributions to health disparities

Health Care System
- Universal access to quality care, (chronic care/team approach model)
- Patient centered approach with sensitivity to the nation's diversity
- Automated eGFR reporting
- Early referral for co-management
- Personalized care, including disease modifiers

Community Level
- Small area analysis to identify community specific needs
- Advocacy for social & health justice
- Increased organ donation, especially from minority communities
- Minimizing adverse social determinants of health
- Re-Conceptualization of health and health care, including health beliefs, practices, and mind-body-spirit.

Semin Nephrol. Author manuscript; available in PMC 2014 September 01.