KI REPORTS
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CKD—Where Have All the Women Gone?

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Kidney Int Rep (2022) **7,** 375–377; https://doi.org/10.1016/j.ekir.2021.11.032

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CKD is a common health problem worldwide, with as many as 10% of the adult population having evidence of kidney disease.[1] Most of these people are unaware of their diagnosis. For most diagnoses, CKD tends to progress inexorably toward the "end-stage"—at which point, subjects require kidney replacement therapy (KRT), meaning dialysis or transplantation, if they have survived. CKD is graded by severity into 5 stages, with stage 1, representing the mildest disease, to stage 5, representing the last vestiges of renal function and eventually the need for KRT.[2] Proteinuria is an important modifier of this process, as heavier proteinuria portends more rapid progression and, as such, has become a target of therapeutic interventions to slow progression.

CKD affects men and women approximately equally, with a likely higher incidence in females, at least as recorded, in the earlier stages. Yet, dialysis and transplant programs are over-represented by men. This is a universal observation; for example, in our own country, the Australian and New Zealand Dialysis and Transplant Association registry reveals that men outnumber women at dialysis entry approximately 7:4.[3] So, where have all the women gone between early and late-stage CKD and what explains this observed difference between the trajectories of men and women diagnosed with having CKD?

This edition of the *KI Reports* contains 2 reports from the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKD-DOPPS) group, which evaluate this question.[4,5] The 2 papers use different approaches to address the reasons for the observed discrepancy between males and females with respect to prevalence of CKD and KRT initiation. The first paper is based on CKD-DOPPS clinics from 4 high- and middle-income countries (Brazil, France, Germany, and United States of America). This analysis reveals that in these clinics, focused on CKD stage 4 and beyond, men again predominate. Men also had a more rapid decline in renal function, partly explaining an over-representation of men at KRT entry. Nevertheless, the paper only addresses the factors affecting disparity in the "post-referral" part of the CKD continuum. It is likely that events before this time have a significant impact on progression and outcome, and little is known on how referral patterns from primary care differ between males and females. This remains an avenue for future quantitative and qualitative research.

The second paper surveyed nephrologists from 22 low-, middle-, and high-income countries for their views on why women are under-represented in the KRT programs. Here, it is important to recognize the differences in sex and gender. Sex here relates to anatomical, genetic, and physiological differences, whereas gender relates to behavior, roles, activities, and attributes determined over time by family, cultural, and societal influences and expectations. The paper identifies common themes of economic inequity and social relationships and family responsibilities as key differences between males and females, suggesting females do face many gender-based barriers to access to care. In addition, based on their thematic analysis, they proposed interventions to address these barriers.

When these papers are considered together, there are a number of interesting observations. Some of the barriers identified thematically in the second paper are also represented in the baseline demographic data from CKD-DOPPS. For example, economic inequity and other related factors, such as access to health insurance, are raised as barriers to equitable access to care by the nephrologists interviewed. Likewise, in the CKD-DOPPS analysis, women were found to be less frequently employed than men. This clearly represents a barrier to access to

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KRT in countries without universal health cover or where health insurance is linked to employment. Similarly, men were more frequently married than women at baseline in the CKD-DOPPS data, perhaps suggesting greater social support networks. Interviews with nephrologists revealed concern that family and other social responsibilities limited women's ability to prioritize their own health and access appropriate care for advanced CKD, including KRT when indicated. As nephrologists, we need to remain cognizant of this and ensure, as much as possible, that the care we provide is equitable and appropriate.

Gender alone is unlikely to explain the whole picture. A number of observations across these 2 studies point to intersectional disparity being important in evaluating the impact of gender on CKD outcomes. Biological factors, such as age, seemed to magnify the gender-based disparity with a lower prevalence of older women in CKD-DOPPS data compared with the CKD prevalence in the general population (National Health and Nutrition Examination Survey) in the United States.[6] Unsurprisingly, differences in social factors also seem to intersect with gender. It is interesting to note that when evaluated individually, the countries involved in the CKD-DOPPS study produced different data. These country-specific differences raise questions on the generalizability of these data beyond those specific countries and their health systems. Nevertheless, these differences also point to social, cultural, and demographic factors being important and difficult-to-measure drivers of disparity. This is reflected in themes identified in the interviews of nephrologists from diverse backgrounds and fits broadly with the intersection of gender-based disparity and social determinants of health.

As an aside, the ratio of reaching KRT or dying was approximately 1:1 in the CKD-DOPPS experience—a different pattern than that reported for large CKD populations, wherein far more patients die before or instead of receiving KRT.[7] This suggests a number of possibilities: (i) care in CKD clinics prevents mortality; (ii) care in CKD clinics is heavily directed toward KRT; and (iii) referrers, such as primary care physicians, are not referring those patients they judge to be unlikely to benefit from KRT. It does raise the issue of whether nephrologists should be more involved in earlier stages of CKD care. Some units specifically operate early CKD clinics to assist primary care providers to establish CKD etiology, consider indications for specific therapy, such as immunosuppression, and ensure initiation of treatment to limit CKD progression and address cardiovascular disease risk. The potential workload of managing this very large group is substantial, so it may be more appropriate to direct our efforts at educating the primary care workforce and our medical students on recognizing the presence of CKD and then managing elements of CKD care, such as blood pressure control and blood pressure targets, blood sugar control in individuals with diabetes, and introduce new concepts, such as the use of the sodium-glucose transport protein 2 inhibitors.[8]

Even before the development of CKD, there are risk factors pertinent to women, which, if recognized and addressed, could reduce rates and/or progression of renal disease. Hypertensive disorders of pregnancy, including pregnancy-induced hypertension and preeclampsia, are associated with an increased risk of future CKD, including CKD5/5D and cardiovascular disease more generally. Globally, the incidence of hypertensive disorders of pregnancy increased from 16.30 million to 18.08 million pregnancies from 1990 to 2019 with a prevalence of 2% to 25%, highest in low-income settings.[9] Identification of these women during childbearing years and before CKD development provides a significant opportunity to intervene early in the disease process and possibly alter their CKD trajectory. This is perhaps of greatest importance in low- and middle-income countries where rates of both hypertensive disorders of pregnancy and gender-based disparity in access to CKD care are highest. Further research into pragmatic and accessible public health interventions is needed.

Finally, it must be noted that although not captured in these data, conservative/supportive care and palliative care are important and appropriate approaches for many patients with advanced CKD. It is well recognized that in people with advanced age and multiple comorbidities, KRT may not prolong life and further may affect detrimentally on quality of life. Equitable access to shared decision-making approaches and good quality symptom management and end-of-life care is a crucial component of the management of people with CKD. Understanding the barriers presented by gender and other social determinants of health to achieving this deserves further evaluation.

It is incumbent on all health care providers to be cognizant of the need to provide patient-centered care based on clinical need and free of inequity based on gender or other sociodemographic factors. There is currently significant gender-based disparity in

CKD outcomes and access to CKD care at all stages of the continuum. This research progresses our understanding of drivers of this disparity, raises numerous avenues for future research, and highlights how we, as nephrologists, might start to meaningfully address these gender-based differences to improve outcomes.

DISCLOSURE

All the authors declared no competing interests.

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