CKD – Where have all the women gone?

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Chronic Kidney Disease (CKD) is a common health problem around the world, 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 towards “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, through 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 shows 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 CKD?

This edition of the Journal contains 2 reports from the CKD-DOPPS group which examine this question [4,5]. The two papers utilise 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 & US). This analysis demonstrates that in these clinics, focused on CKD Stage 4 and beyond, men again predominate. Men also showed a more rapid decline in renal function, partly explaining an over-representation of men at KRT entry. However, the paper only addresses the factors affecting disparity in the ‘post referral’ part of the CKD continuum. It is likely that events prior to this time have a significant impact on progression and outcome and little is known about 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 KRT programs. Here it is important to recognise the differences in sex and gender. Sex here relates to anatomical, genetic and physiological differences; whereas gender relates to behaviour, 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 that 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 is raised as a barrier to equitable access to care by the Nephrologists interviewed. Likewise, in the CKD-DOPPS analysis, women were shown to be less frequently employed than men. This clearly represents a barrier to access to kidney replacement therapy 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 prioritise their own health and access appropriate care for advanced CKD, including kidney replacement therapy when indicated. As Nephrologists we need to remain cognisant 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 two studies point to intersectional disparity being important in assessing the impact of gender on CKD outcomes. Biological factors such as age
appeared to magnify the gender-based disparity with a lower prevalence of older women in CKD-DOPPS data compared with general population CKD prevalence (NHANES) in the United States [6]. Unsurprisingly, differences in social factors also appear to intersect with gender. It is interesting to note that when examined individually, the countries involved in the CKD-DOPPS study produced different data. These country-specific differences raise questions about the generalisability of this data beyond those specific countries and their health systems. However, 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: 1) care in CKD clinics prevents mortality; 2) care in CKD clinics is heavily directed towards KRT; 3) 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 aetiology, 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 recognising the presence of CKD and then managing elements of CKD care such as blood pressure control and blood pressure targets, blood sugar control in diabetics, and introduce new concepts such as the use of the SGLT2 inhibitors [8].

Even prior to the development of CKD, there are risk factors pertinent to women which, if recognised and addressed, could reduce rates and/or progression of renal
disease. Hypertensive disorders of pregnancy (HDP) including pregnancy-induced hypertension and pre-eclampsia are associated with an increased risk of future CKD including CKD5/5D, as well as cardiovascular disease more generally. Globally, the incidence of HDP increased from 16.30 million to 18.08 million pregnancies from 1990 to 2019 with a prevalence of 2-25%, highest in low-income settings [9]. Identification of these women during childbearing years and prior to 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 HDP and gender-based disparity in access to CKD care are highest. Further research into pragmatic and accessible public health interventions are needed.

Finally, it must be noted that while not captured in this data, conservative/supportive care and palliative care are important and appropriate approaches for many patients with advanced CKD. It is well recognised that in people with advanced age and multiple co-morbidities, KRT may not prolong life and further, may impact 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 examination.

It is incumbent on all health care providers to be cognisant of the need to provide patient-centred care based on clinical need and free of inequity based on gender or other socio-demographic 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.

Disclosures
Nothing to disclose
REFERENCES:


