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Is There Still a Place to Study Race in the Nephrology Space?

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In a recent issue of *KI Reports,* Ling *et al.*[1] examine the differences in the incidence of end-stage kidney disease (ESKD) and mortality between a Southeast Asian (SEA) and White population living in the UK and Wales. Chronic kidney disease (CKD) affects >10% of the world's population, or approximately 850 million individuals. In fact, CKD has emerged as one of the leading causes of mortality worldwide, with an increasing number of associated deaths over the last 2 decades.[2] A CKD diagnosis can have a significant impact on patients' health and wellbeing. Identifying high-risk groups could lead to earlier recognition of individuals in whom treatment could modify kidney disease progression.

The authors undertook this study after noting the UK registry data consistently showed that minority ethnic groups were disproportionately represented among patients with a diagnosis of ESKD and kidney replacement therapy with either dialysis or transplant. Previous data suggested that Asian ethnicity was a risk factor for CKD progression; however, there is a fair amount of inconsistency in the published literature about the amount of risk, or whether it exists at all.[3] In an attempt to identify high-risk persons, the authors compared a primary care cohort of self-identified SEA patients with White patients to evaluate the impact of estimated glomerular filtration rate (eGFR) by sex and ethnicity, accounting for cardiovascular comorbidities. The authors were able to make use of the large Clinical Practice Research Datalink to extract data from 35 million patient records. Ultimately, they identified 40,888 SEA and 236,634 White patients for comparison.

First, identification of high-risk groups could be beneficial to individuals, as well as the healthcare system as a whole. If certain ethnic groups were shown to have higher overall risk for kidney disease progression, resources could be allocated to improve outcomes. In addition, community outreach programs could be initiated to create educational material that is cultural and language specific. Free screening and financial support of treatments that slow disease progression could have a significant economic impact at the national level. Finally, genetic evaluation and proteomics of certain high-risk groups might help identify unique targets for treatment, similar to inaxaplin for patients with APOL1 gene associated focal segmental glomerulosclerosis.[4]

On the other hand, there has been much debate about race classification in medical research and clinical care. In the era of precision medicine, race may become irrelevant as a proxy for ancestry. Sociologists have long argued that race is arbitrary, based on social rather than biological constructs. Despite associations between specific gene variants and certain races, race designations accurately only reflect a portion of ancestral differences in genotype. In this paper, the authors combine SEAs (Bangladeshis, Indians, and Pakistanis) into a single racial group. In the US, self-reported Black patients are similarly placed into a single group despite a quarter of ancestry markers identifying Black individuals as non-African origin.[5] No ethnic or racial group is a monolith, and differences in culture (diet, exercise, language, and education) may also play heavily into health care utilization and outcomes. Finally, given immigrants' assimilation into their adopted country's culture, it would be difficult to compare rates and risk factors for ESKD in this UK cohort with other groups of SEAs living elsewhere.

Focusing on a single variable, such as ethnicity or race, to determine disease risk is likely an oversimplification of a complex process. CKD risk and progression are multifactorial and include environmental and socioeconomic factors that often disproportionately affect minority groups (nature vs. nurture). For comparison, in the US there are significant disparities in

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CKD rates and outcomes between Black and White patients. Similar to the UK, minority groups are overrepresented in the US ESKD population. There are many reasons for disparities in CKD outcomes. For instance, patients with ESKD who are from non-White racial and ethnic groups in the US more often experience delays (for a multitude of reasons) in initial referral to nephrology specialists. However, access to health care is not the only reason for such disparities. In fact, in a study of Black Americans in the military, the existence of CKD disparities by median household income suggested that social issues contribute to health disparities, despite access to universal health care coverage.[6] Identification of barriers to healthcare access is as essential as identification of at-risk populations, when trying to make a decisive impact on patient outcomes.

Another recent controversy surrounding race and CKD management involves the use of race-based equations for estimating glomerular filtration rate. Raced-based eGFR equations are fraught with problems, not the least of which is mixed race individuals. The authors of this paper explicitly excluded these individuals from evaluation in this study. Use of race-based equations has led to disparities in referral for transplantation, due to overestimations of eGFR in some groups, including SEAs.[7] In a retrospective analysis of 8 US cohorts including Black and non-Black individuals, the eGFR equation without race that included creatinine and cystatin C demonstrated racial differences in the risk of kidney replacement therapy and mortality throughout the range of eGFR.[8] The authors do address this issue, using a CKD-EPI-PK equation developed in a Pakistani population, that has shown improved accuracy in SEA individuals. When the CKD-EPI-PK equation was used the hazard ratio for ESKD was significantly lower in SEA males versus White males, but the overall relationship of eGFR to outcomes was unchanged.

Overall, the results of this study suggest that SEAs living in the UK do not experience a substantially higher rate of ESKD than the White population in the UK and Wales. In addition, registry data suggested SEA patients may survive longer than Whites receiving kidney replacement therapy. Increased survival on dialysis is also seen in the US in Black versus White patients, and whereas some have attributed this to a higher number of more severe comorbid conditions in the White dialysis population, the reasons for this remain unclear.[9] Although the study did not show that SEA patients are a high risk-population, the disproportionate number of SEA patients with ESKD or kidney replacement therapy suggests that this group would benefit from additional pre-ESKD preventive resources.

In conclusion, efforts to reduce racial disparities in CKD may additionally provide models for reducing disparities among other high-risk, underserved populations. It is incumbent upon nephrologists to understand not only the pathophysiology of CKD, but also how social factors and cultural differences may influence disease management. Although medical classification by race may have a role in identifying and addressing disparities, race is an imperfect marker for genetic and cultural variation. In research and in clinical practice, use of race categories must be accompanied by an understanding of their limitations.

DISCLOSURE

The author has declared no competing interests.

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