



## EDITORIAL COMMENT

# Burden, access and disparities in kidney disease: chronic kidney disease hotspots and progress one step at a time

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The 2019 International Society of Nephrology World Kidney Day theme is Kidney Health for Everyone Everywhere. It focuses on the uneven burden of acute kidney injury and chronic kidney disease (CKD) in different communities, identifies disparities and challenges in access to care and calls for universal health coverage for prevention and early treatment of kidney disease. This topic is fully in line with the *Clinical Kidney Journal* (*ckj*) editorial strategy for improving worldwide kidney care without leaving any community behind. Indeed, the first PubMed-recorded use of the term CKD hotspot was in *ckj*, where it was defined as ‘countries, region[s], communities or ethnicities with higher than average incidence of CKD’. This issue of *ckj* contains the World Kidney Day editorial as well as contributions that illustrate two concepts: the need to validate biochemical thresholds generated in developed countries in other populations, as exemplified by Kidney Disease: Improving Global Outcomes CKD–mineral and bone disorder parameters in an African population, and the fact that some disease associations characteristic of developing countries may be described initially in developed countries, as exemplified by the association of *APOL1* variants with CKD or by minimal change disease secondary to malaria, but have to be validated locally.

**Keywords:** *APOL1*, chronic kidney disease hotspot, hypertensive nephropathy, malaria, PTH, vitamin D

The 2019 International Society of Nephrology Kidney Day theme is Kidney Health for Everyone Everywhere. It focuses on the uneven burden of acute kidney injury and chronic kidney disease (CKD) in different communities, identifies disparities and challenges in access to care and calls for universal health coverage for prevention and early treatment of kidney disease [1]. As reflected in the World Kidney Day editorial published in this issue of *Clinical Kidney Journal* (*ckj*) [2], *ckj* has contributed and continues to contribute to a better understanding of the burden and nature of kidney disease in developing countries as well as disparities in access and outcomes between and within countries.

The first conceptualization of the term ‘CKD hotspots’ recorded in PubMed was published in *ckj*, where it was defined as ‘countries, region[s], communities or ethnicities with higher than average incidence of CKD’ [3]. The ultimate aim of the term was to draw attention to the plight of persons at high risk of CKD within these hotspots. Indeed, the second PubMed-recorded use of the term was also in *ckj*, illustrating CKD hotspots in developing countries in South Asia [4]. The current issue of *ckj* contains several examples that contribute to a better understanding of the burden of kidney disease in developing countries, raising the issue of how clinical concepts generated in developed countries should be validated in populations

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around the world. Ideally, enough funding should be provided not only to facilitate universal access to care but also to fund studies that allow population-specific clinical concepts to be first generated from within developing countries where these concepts apply.

Sumaili *et al.* [5] characterized the association of APOL1 alleles with CKD and end-stage renal disease, and specifically with hypertension-attributed nephropathy in Central Africa. Trypanolytic APOL1 variants were first associated with the high incidence of CKD in US patients of African ancestry 9 years ago and were shown to be mostly associated with human immunodeficiency virus nephropathy and hypertension-attributed CKD [6]. Initially the question remained open whether, in Africa, where these specific genetic variants had propagated in response to environmental pressures, they were also associated with CKD, given the different lifestyles and environments. Sumaili *et al.* [5] largely confirm the association between trypanolytic APOL1 variants and CKD in Kinshasa (Democratic Republic of Congo): subjects carrying two risk alleles had an adjusted odds ratio of 7:7 for hypertension-attributed nephropathy, in line with American studies. However, the high-risk APOL1 genotypes were G1/G1 and G1/G2, whereas G2/G2 was not found in the study population, which differed from the higher frequency of G2/G2 in the USA. The authors hypothesize that the absence of G2/G2 is consistent with environmental pressures since this allele combination increases the susceptibility to severe *Trypanosoma brucei gambiense* infection. The finding is conceptually significant since it illustrates that findings in developed countries can be reproduced in developing countries, despite differences in socio-economic status and lifestyle, but that local differences do exist that should be characterized to improve patient care.

Cavalier *et al.* [7] explore another key issue: to what extent do biochemical thresholds generated in developed countries apply to other populations. They established the upper limit of normal of parathyroid hormone (PTH) concentration in healthy persons from the Ivory Coast and evaluated the prevalence of vitamin D deficiency, which was low. Interestingly, the relationship of the upper limit of normal of PTH concentration in the Ivory Coast with that in Caucasians depended on the specific PTH assay used and was similar only for third-generation PTH assays. The impact of validating thresholds and equations in different population goes well beyond CKD–mineral and bone disorder. Thus, although not mentioned in a seminal manuscript discussing the reasons to determine measured rather than estimated glomerular filtration rate (mGFR and eGFR, respectively) [8], the most widely used and Kidney Disease: Improving Global Outcomes–recommended equation to assess eGFR, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation, has an adjustment for race, and specifically for black race, that may not apply to black ethnicity outside the USA and Europe [9, 10]. This creates confusion when estimating the prevalence of CKD outside the USA and Europe, and more specifically in Africa, where lack of high-quality epidemiological studies is a major issue, as emphasized by the World Kidney Day editorial [2]. Specifically, in South Africa, this equation and the Modification of Diet in Renal Disease equation are used without adjustment for ethnicity because of evidence that they perform better that way [11, 12]. Indeed, although the CKD-EPI creatinine equation without the correction factor performed better in black South Africans, none of the CKD-EPI equations attained the 2002 Kidney Disease Outcomes Quality Initiative benchmark of accuracy of eGFR within 30% of mGFR

for 90% of patients, illustrating the need for local research efforts [12]. Use of the CKD-EPI creatinine equation overestimated the prevalence of CKD G5 from 6% to 12%, as assessed by mGFR [12]. This should be kept in mind when interpreting reports such as a recent report from rural Tanzania that disclosed a 12% prevalence of CKD G3–G5 with a strikingly high incidence of CKD G5 of >4% in younger individuals (<26 years old) [13]. The CKD-EPI creatinine equation was used and it should be assumed that the race coefficient was applied, as the authors discuss this coefficient and do not indicate that it was not applied.

A third article illustrates another issue: how can we learn about renal disease in developing countries from kidney disease in travellers from high-income countries? From the USA, Rangwani *et al.* [14] present a rare case of minimal change disease secondary to *Plasmodium falciparum* in a woman who developed nephrotic-range proteinuria and acute renal failure requiring renal replacement therapy after recent travel to Sierra Leone. A careful electronic microscopy study of the kidney biopsy was key to identifying the widespread foot process effacement and podocytopathy that allowed the diagnosis of minimal change disease. Access to this technology is limited even in developed countries, and the diagnosis may have been missed had the patient remained in Sierra Leone. One month after initiating antimalarial treatment, the podocytopathy improved and completely resolved after 6–8 weeks.

Beyond the specific topic of World Kidney Day of disparities in burden and access, ckj has also published regarding disparities in outcomes. Specifically, we looked at recent evidence that socio-economic factors are not only associated with faster progression of CKD, but also with higher mortality among CKD patients even within European countries with ready access to nephrology care [15]. We focused mainly on patients reaching end-stage renal disease and starting renal replacement therapy [16]. Concerning the many potential factors involved, from education to lifestyle to access to specific forms of care, recent attention has focused on environmental factors and more specifically on pollution [17].

In conclusion, disparities in the burden of kidney disease and access to nephrology care are major hurdles to decrease the high death toll from kidney disease worldwide. Universal health coverage for prevention and early treatment of kidney disease would be a giant step toward improving global kidney health. However, ideally this should be complemented with local direct research efforts within more disadvantaged countries or communities, precluding the need to extrapolate concepts generated in developed countries that may apply only partially. This should help us understand and correct the drivers of persisting disparities in outcomes, even in countries with universal coverage.

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## CONFLICT OF INTEREST STATEMENT

None declared.

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