Reducing major risk factors for chronic kidney disease

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Chronic kidney disease (CKD) is a global public health concern and a key determinant of poor health outcomes. While the burden of CKD is reasonably well defined in developed countries, increasing evidence indicates that the CKD burden may be even greater in developing countries. Diabetes, hypertension, and obesity are major contributors to the global burden of the disease and are important *traditional* CKD risk factors; however, *nontraditional* CKD risk factors such as nephrotoxin exposure, kidney stones, fetal and maternal factors, infections, environmental factors, and acute kidney injury are also increasingly being recognized as major threats to global kidney health. A broad approach to CKD prevention begins with the identification of CKD risk factors in the population, followed by the development of appropriate mitigation strategies. Effective prevention policies rely on an accurate understanding of the incidence and prevalence of CKD in a given setting, as well as the distribution and burden of risk factors. Populations or individuals at CKD risk must be screened and treated early to prevent the onset of and delay the progression of the kidney disease. Systematically collected data should be analyzed at country, province, and district levels to identify regional disparities and CKD hotspots and develop targeted prevention strategies. Race-ethnicity, genetics, sex, socioeconomic status, and geography are likely modifiers of CKD risk. A comprehensive, informed approach to prevention that takes into account all of these factors is therefore required to successfully tackle the global CKD epidemic.

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Chronic kidney disease (CKD) is increasingly recognized as a global public health concern and an important contributor to morbidity and mortality.[1] While the burden of CKD is reasonably well defined in developed countries, increasing evidence indicates that the CKD burden may be even greater in developing countries.[1,2] Of the major contributors to the global burden of disease, diabetes, hypertension, and obesity are *traditional* risk factors for CKD.[1] *Nontraditional* CKD risk factors such as nephrotoxins (e.g., prescription medicines and alternative remedies), kidney stones, fetal and maternal exposures, infections, environmental exposures, and acute kidney injury (AKI) are also being increasingly recognized as major threats to kidney health.[3] The burden of CKD that is attributable to nontraditional risk factors is unknown and may even predominate in low- and middle-income countries (LMICs).

A broad approach to CKD prevention begins with the identification of the incidence, prevalence, and distribution of

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risk factors, followed by the development of mitigation strategies. At-risk populations or individuals must be screened and treated early to prevent onset and delay progression. Reducing CKD risk is also highly dependent on addressing the fact that it is both a consequence of and a contributor to socioeconomic disparities. This review expands on the recently published International Society of Nephrology (ISN) CKD roadmap,[4] which discusses the globally relevant major traditional and nontraditional risk CKD factors (outlined in Table 1), highlights gaps in knowledge, and recommends strategies to close these gaps and enhance CKD prevention.

Prioritization of CKD and detection and investigation of CKD hotspots

To understand whether CKD is a priority within a country, incidence and prevalence, as well as the contribution of various risk factors for the burden of disease should be determined. Systematic and reliable data collection is required. It is important that such data are analyzed at region, country, province, and district levels to identify local disparities and CKD hotspots. For example, the global burden of disease study has identified several hotspots in Central America where the prevalence of CKD is high and requires attention.[5–7] These include Mexico, where women have one of the highest disability-adjusted life-year rates for CKD (related to obesity, diabetes, and hypertension), as well as pockets in Nicaragua, Guatemala, and El Salvador, where CKD of unspecified cause is highly prevalent in men, primarily related to nontraditional risk factors.[7,8]

To illustrate the importance of subregional local analysis, in Nicaragua, increased CKD rates in male farmers aged <60 years were associated with pesticide exposure, dehydration, alcohol consumption, and exposure to heavy metals.[9] Costa Rica has reported a higher incidence of CKD among young sugarcane workers, with clinical and histological findings of chronic interstitial nephritis.[10] In El Salvador, a high prevalence of CKD (17%) was observed among male farmers exposed to toxic pollutants.[11,12] Studies in Sri Lanka reported an association between pesticide poisoning and pollutants, with repeated episodes of AKI and CKD.[13] In India and Pakistan, a large percentage of CKD cases are of undetermined etiology, potentially related to environmental factors.[14] Many knowledge gaps remain regarding these regional epidemics of CKD of unspecified cause.[5]

Gaps. There are no reliable statistics about the prevalence of CKD in most of the developing world. Improving and expanding local data collection and processing and research infrastructure is recommended to ensure a better understanding of the burden and regional distribution of specific CKD risk factors.

Action strategies. Including screening for kidney disease in established noncommunicable disease (NCD) risk factor surveys will add significant value to existing efforts to monitor the prevalence of NCD risk factor, likely at a lower cost than duplicating efforts with parallel CKD surveillance programs. Combining such survey data with global positioning technology will permit the identification of regional and local variations in CKD occurrence. For example, the World Health Organization (WHO) STEPwise approach to surveillance is an NCD household survey that was launched in 2002.[15] To date, 122 countries have participated.[16] Depending on the local resources, the survey collects behavioral risk factors (step 1); physical measurements, including blood pressure (BP), height, and weight (step 2); and biochemical parameters (blood glucose and lipids; step 3).[17] Advocacy efforts in Uruguay succeeded in including serum creatinine and urine protein measurements in the STEPwise approach to surveillance survey in 2006. This effort captured the attention of policy makers and resulted in a policy mandating kidney disease screening in individuals with hypertension or diabetes at regular health checkups in the employed population. This program is raising CKD awareness and will permit tracking of prevention efforts.[18]

Importantly, surveillance or outreach activities must include vulnerable groups and ensure equitable representation of the population. Monitoring activities should integrate national data at regional and local levels with data obtained in research and screening activities to optimize efficiency, facilitate surveillance, and permit the rapid identification of geographic hotspots for CKD that require focused attention.[19] A task force supported by global experts should be setup to investigate hotspots rapidly. Investigations should include standardized data on social, structural, and clinical risk factors, clinical course, and potential interventions. A guideline-based approach should be disseminated and adapted in regions experiencing CKD hotspots. An example is the international study group on CKD of unspecified cause in Mesoamerica, organized by the Central American Program for Work, Environment, and Health.[20] Such efforts require a multi-sectoral approach with sustainable financing.[21]

Tackling CKD risk factors: diabetes, hypertension, and obesity

The WHO global action plan for the prevention and control of NCDs does not include CKD among the four priority NCDs. However, diabetes, hypertension, and cardiovascular disease (CVD) are acknowledged to be integrally linked with CKD. Notably, CKD is an important risk amplifier within these conditions.[22] Across the world, 415 million adults have diabetes, 1.4 billion adults have hypertension, and 2.1 billion children and adults are overweight or obese.[23–25] The prevalence of CKD in adults with type 2 diabetes is approximately 25% to 40%, depending on population factors.[26–28] In the United States, the prevalence of CKD is approximately 30% among adults with hypertension and 17% among obese adults.[26] The size of the population at CKD risk is influenced by regional differences in demographics, different approaches to diagnosis and management, and effectiveness of local interventions to address lifestyle-related risks. Reduction of lifestyle-related risks is a cornerstone of mitigating the public health impact of diabetes, hypertension, and obesity. There is clear evidence that links upstream factors such as poor diet, poverty, food insecurity, tobacco consumption, and other