Air Pollution and Kidney Disease

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CJASN 15: 301–303, 2020. doi: https://doi.org/10.2215/CJN.16031219

In the past several decades, a lot of attention was focused on individual-level risk factors for kidney disease, and for so long the relationship between environmental exposures and kidney disease has not been seriously examined. Recent advances in nanomedicine enabled studies in rodents and humans showing that inhaled gold nanoparticles, when sufficiently small, permeate through the lung alveolar tissue and enter the bloodstream where they interact with extrapulmonary organs, are filtered by the kidneys in a size-dependent manner, and ultimately excreted in the urine (1). These proof-of-principle studies demonstrated for the first time that inhaled aerosols may come in contact and potentially interact with kidney tissue (1). Recently, experimental evidence has emerged suggesting that rodents exposed by inhalation to diesel exhaust particles (to experimentally simulate exposure to fine particulate matter air pollution) exhibited increased oxidative stress, inflammation, and DNA damage in kidney tissue. After prolonged exposure, these rodents exhibited structural chronic kidney injury manifested by vascular damage, glomerular sclerosis, mesangial expansion, and tubular atrophy (2,3). These findings provided biologic plausibility for a putative injurious effect of aerosol pollution on the kidney and powered the generation of hypotheses to test the effect of fine particulate matter air pollution on risk of kidney disease in humans.

Several large epidemiologic studies have since emerged suggesting that ambient fine particulate matter of <2.5 μm in aerodynamic diameter ($PM_{2.5}$) air pollution is associated with increased risk of incident CKD, CKD progression, and ESKD (4,5). Recent studies also provided evidence that $PM_{2.5}$ pollution is associated with increased risk of death due to kidney disease (6). It is estimated that 17%–20% of the global toll of CKD burden may be attributable to $PM_{2.5}$ pollution, and that the burden is unevenly distributed geographically and is more heavily tilted toward low and low-middle income countries, which might be least equipped to deal with the adverse health consequences of air pollution (7). Other aerosols including ambient coarse particulate matter of ≤ 10 μm in aerodynamic diameter, nitrogen dioxide, and carbon monoxide have also been associated with increased risk of incident CKD and its progression to ESKD (8).

Environmental Injustice

Beyond its effect on the kidneys, $PM_{2.5}$ air pollution contributes to 8.9 million deaths per year globally, and it does so discriminately. Studies on the health effects of ambient air pollution paint a story of environmental injustice. Evidence suggests profound racial and nonracial socioeconomic disparities in $PM_{2.5}$-associated burden of disease—a reflection of the influence of several factors including differences in $PM_{2.5}$ exposure, and differential susceptibility to a given level of exposure (6). In the United States, black individuals and people living in socioeconomically disadvantaged communities are exposed to higher levels of $PM_{2.5}$ air pollution. And for the same level of $PM_{2.5}$ exposure, black individuals and people living in disadvantaged communities are more vulnerable (exhibit higher risk and thus are more sensitive) to the adverse health outcomes associated with $PM_{2.5}$ exposure, further compounding their risk (6). In the United States, racial minorities experience a "pollution disadvantage" as they are exposed to 56%–63% more pollution than is caused by their consumption, whereas non-Hispanic whites experience a "pollution advantage" of 17% less pollution exposure than caused by their consumption. This difference between the pollution experienced by a racial-ethnic group and the pollution caused by their consumption represents "pollution inequity," which remains high despite progress in reducing $PM_{2.5}$ pollution in the United States.

Neighborhood air quality is not only influenced by local emissions, but is also governed by transboundary forces including long-distance pollutant atmospheric transport and international trade. For example, because of atmospheric transport of pollutants, 47.2% of the >8000 pollution-related deaths that occurred in Canada in 2007 were caused by emissions produced in the United States (9). Because of international trade, 29.7% of the nearly 200,000 $PM_{2.5}$-related deaths in Eastern Europe in 2007 were caused by emissions related to good and services consumed in Western Europe, and nearly 11% of the more than 1 million deaths that occurred in China in 2007 were caused by emissions related to goods and services consumed in Western Europe and United States (9). On average, about 12% of the global premature deaths related to $PM_{2.5}$ pollution are attributable to air pollutants emitted in a geographic region other than that in which the death occurred, and about 22% of global deaths attributable to $PM_{2.5}$ pollution are associated with goods and services produced in one region for consumption in another (9).

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More Evidence of Air Pollution and the Kidney

Although a body of evidence has amassed on the association between $PM_{2.5}$ and other aerosols and kidney disease (8), more high-quality, epidemiologic cohort studies are still needed to better characterize exposure-response functions in different populations, and to more accurately estimate the burden of kidney disease attributable to air pollution. In this issue of *CJASN*, a research article by Blum *et al.* (10) aimed to examine the association between average annual $PM_{2.5}$ exposure and kidney disease in a cohort of 10,997 participants from the Atherosclerosis Risk in Communities project. The study is notable for many reasons. First, this is a study first-authored by a trainee who should be commended on undertaking this line of investigation. Recognition should also be accorded to his mentors (Grams and others) for supporting this effort, and to the *CJASN* editorial team for establishing a mechanism—the *CJASN* Trainee of the Year Award Program—to encourage manuscript submissions and promote visibility of original kidney research produced by trainees. Blum *et al.* showed, in cross sectional analyses, an association between higher $PM_{2.5}$ and albuminuria. More interestingly, in longitudinal analyses of 10,302 cohort participants followed for median of 17.7 years, there was a significant association between $PM_{2.5}$ and risk of CKD. Analyses to characterize an exposure-risk function suggested a near linear increase in risk across the spectrum of $PM_{2.5}$ concentrations in this cohort. This effort is meritorious in that it builds more evidence to further illuminate our understanding of the effect of $PM_{2.5}$ on risk of kidney disease; data from this study will contribute to the ongoing effort to more accurately estimate burden of CKD attributable to air pollution.

Despite progress in generating new knowledge on the relation of $PM_{2.5}$ and CKD over the past few years, significant knowledge gaps remain. As most of the evidence on this matter was derived from studies conducted in North America where $PM_{2.5}$ levels are lower than other areas of the world; high-quality, large cohort studies from East Asia, India, Southeast Asia, Northern Africa, Eastern Europe, and Russia (which have higher levels of $PM_{2.5}$) are still needed to gain a better understanding of the characteristics and morphology of the relationship between $PM_{2.5}$ and kidney disease across the concentrations of $PM_{2.5}$ experienced by humans worldwide. Prior studies on the health effects of $PM_{2.5}$ did not consider composition and toxicity of the components of these fine particles, careful analyses of the health effects (and kidney effects) of $PM_{2.5}$ components will inform more efficient mitigation strategies.

The broader implications of this body of research are clear: there is an increasing recognition that in addition to individual risk factors, contextual determinants including environmental risk factors are important drivers of burden of noncommunicable diseases (NCDs) including kidney disease. In September 2019, the United Nations high-level meeting on NCDs expanded its priority list of risk factors for NCDs from the previous four individual risk factors (tobacco, alcohol, unhealthy diet, and physical inactivity) to now include a fifth risk factor: air pollution. The emergence of evidence on the relation between air pollution and CKD, and the rapidly increasing burden of CKD, represent pressing priorities that should be reflected on the global health agenda.

Evidence overall suggests that air pollution is an important risk factor for the development and progression of kidney disease, and the global burden of kidney disease attributable to $PM_{2.5}$ air pollution is substantial. The burden of health loss attributable to air pollution is disproportionally borne by the disadvantaged—a story of environmental injustice endured by so many, yet largely invisible—driven in the United States by racial pollution inequity, and globally by the transboundary forces of atmospheric transport and growing international trade. Better awareness of air pollution as a major contributor to NCDs in general, and to kidney disease specifically, is important. And beyond public awareness, integration of $PM_{2.5}$–CKD as a risk–outcome pair in the global evaluation of burden of health loss attributable to air pollution will be an important next step. Stakeholders with interest in reducing the burden of kidney disease and addressing health disparities should actively participate in addressing knowledge gaps and driving policy discussions aimed at developing better approaches to mitigate health loss due to air pollution at both the local levels and globally.

Acknowledgments

The contents do not represent the views of the US Department of Veterans Affairs or the US Government.

Disclosures

Dr. Al-Aly and Mr. Bowe have nothing to disclose.

Funding

This work was supported by funds from the Institute for Public Health at Washington University in St Louis.

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Published online ahead of print. Publication date available at www.cjasn.org.

See related Article, "Particulate Matter and Albuminuria, Glomerular Filtration Rate, and Incident CKD," on pages 311–319.