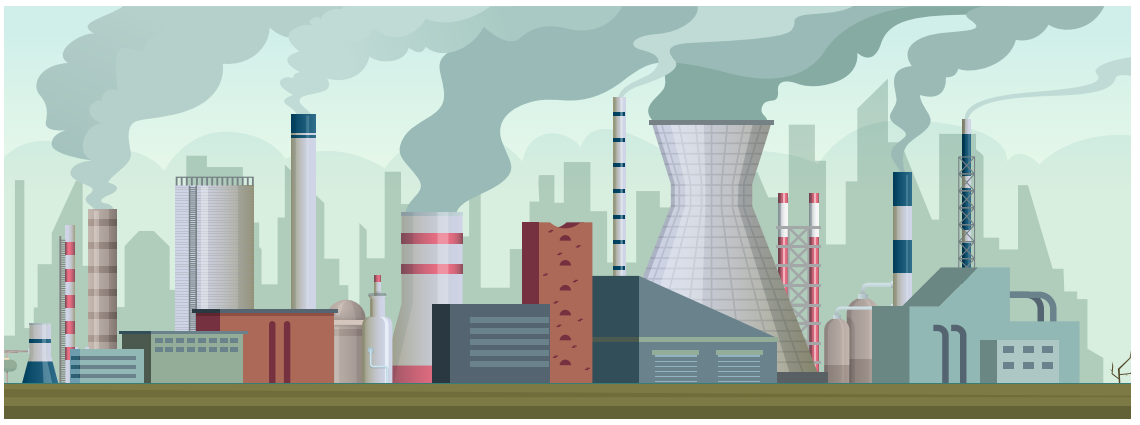
Fine Particulate Matter Air Pollution Is a Risk Factor for Kidney Failure in Patients with IgA Nephropathy

By Rose Mary Attieh



Despite decades of research, our understanding of the pathophysiology of immunoglobulin A (IgA) nephropathy and the risk factors predicting progression to kidney failure remains incomplete. A multi-hit mechanism has been proposed, necessitating a trigger by certain bacterial or viral infections in a genetically predisposed individual (1).

Since galactose-deficient (Gd)-IgA production is believed to be related to mucosal immune dysfunction of the respiratory tract (2), an innovative clinical investigation recently published in *Kidney International* by Luo et al. examined the effect of air pollution, as measured by exposure to fine particulate matter <2.5 µm in diameter (PM2.5), on the risk of kidney failure in patients with IgA nephropathy (3).

This study enrolled 1979 patients with biopsy-proven IgA nephropathy in China. The investigators used satellite data to evaluate PM2.5 exposure in different Chinese regions from 1998 until 2016. The trends in PM2.5 exposure, incidence of end stage kidney disease (ESKD) at 5 years after study enrollment, and estimated glomerular filtration rate (eGFR) decline were compared between provinces. Patients residing in north provinces had a higher burden of exposure to PM2.5 compared with south residents. The provinces with the highest PM2.5 exposures clearly had faster rates of eGFR decline and higher incidence of ESKD. Each 10 µg/m^3 increase in annual average concentration of PM2.5 exposure before study entry led to a 14% increase in risk of ESKD, and each 10 µg/m^3 increase in time-varying PM2.5 exposure after study entry increased the risk of ESKD by 10%. Above-median PM2.5 pollution exposure both before and after study entry increased the risk of ESKD by 54%. The associations held after the authors adjusted the models for lab/clinicopathologic covariates known to affect outcomes in IgA nephropathy, as well as time period, city size, and cardiovascular risk factors. City size was used as a proxy for socioeconomic status, given their known correlation in China. The authors concluded that PM2.5 is an independent risk factor for kidney failure in patients with IgA nephropathy.

This study moves the field further by proposing that an incremental dose-response relationship exists between pollution and the progression of kidney diseases in IgA nephropathy, thus reinforcing similar findings in the general chronic kidney disease population (4) and in patients with membranous nephropathy (5).

This study has many limitations. First, there was a lack of ethnic diversity within the studied cohort. Socioeconomic status and access to health care were inferred by city size. Moreover, there are significant limitations that made it impossible to objectively measure an individual's actual particulate exposure, which depends on multiple factors such as the residence's proximity to air pollution sources, indoor air pollution, time spent outside, or potential change in address after enrollment, for example. Furthermore, the low number of participants with available serum Gd-IgA levels could explain the lack of effect of serum Gd-IgA1 levels on ESKD progression in either PM2.5 exposure group.

Although they would need to be confirmed in subsequent studies with multi-ethnic cohorts, the results of this clinical investigation are most certainly thought provoking. Future work should be directed to provide insight into the exact pathophysiology by which air pollution can alter mucosal IgA galactosylation and how this is influenced by an individual's genetic background. Other polluting toxins, such as heavy metals, industrial agricultural chemicals and pesticides, and secondhand smoke, also need to be examined. Such information may help guide regulatory strategies to reinforce pollution control and prevent exposure to populations at risk. ■

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The author reports no conflicts of interest.

Effect of exposure to particulate matter <2.5 µm in diameter (PM2.5) on progression of IgA nephropathy

KidneyNews

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Kidney centers in China

Biopsy-proven IgA nephropathy (IgAN)

1998–2016

n = 1979
(males 994)

PM2.5 exposure
(derived from satellite aerosol optical depth data)

The PM2.5 exposure levels for patients from different provinces varied.

PM2.5 exposure levels among patients from the north were higher than those among patients from the south.

PM 2.5

The severity of PM2.5 exposure in different regions was correlated with regional kidney failure burden.

HR 1.14
(95% CI 1.06-1.22)

Each 10 µg/m^3 increase in annual average concentration of PM2.5 exposure before study entry was associated with increased kidney failure risk.
(after adjustment for age, gender, eGFR, urine protein, uric acid, hemoglobin, mean arterial pressure, Oxford classification, glucocorticoid, and RASi therapy)

Conclusion The results suggest that PM2.5 is an independent risk factor for kidney failure in patients with IgAN, but these findings will require validation in more diverse populations and other geographic regions. RASi, renin-angiotensin system inhibitor.

Chengwen Luo, Yan Ouyang, Sufang Shi, et al. **Particulate matter of air pollution may increase risk of kidney failure in IgA nephropathy.** *Kidney Int* 2022 Dec;102(6):1382–1391. doi: 10.1016/j.kint.2022.08.020

Visual Graphic by Edgar Lerma, MD, FASN

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