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Editorial Comment

EDITORIAL COMMENT

Increase in the global burden of chronic kidney disease: might it be attributable to air pollution?

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ABSTRACT

Air pollution is an emerging etiology of chronic kidney disease (CKD). Evidence regarding this causative relationship has been shown by several studies. Recently, Lin *et al.* conducted the first community-based study investigating the association between CKD prevalence and air pollutant levels utilizing a Fuzzy Logic Interference model. Despite the study's limitations, the results correlate with the previous meta-analysis and observational studies. Higher fine particular matter (PM2.5) levels are associated with the increased global burden of CKD and may also influence the unequal distribution of burden in low-to-middle income countries. Despite growing evidence of the association of air pollution with CKD risk, the underlying pathophysiology has yet to be fully understood. Future studies investigating the pathophysiology and efficiency of the potential therapeutic and preventive measures against air pollution-related kidney injury are required to reduce the CKD burden.

Keywords: air pollution, chronic kidney disease, PM2.5

Lin *et al.* investigated the long-term effects of air pollution on chronic kidney disease (CKD) prevalence via analyzing the levels of PM2.5, nitrogen dioxide and sulfur dioxide of a town in Taiwan between 2006 and 2016 by utilizing the Fuzzy Logic Inference (FIS) model [1]. Multiple comorbidities such as chronic obstructive pulmonary disease, malignancies, asthma, and some neurological and psychiatric conditions have been linked to air pollution that includes materials with a particulate matter between 2.5 (PM2.5) and 10 micrometers (μm) (PM10) [2–4]. The data regarding the association between air pollution and CKD has been recently emerging, with multiple ongoing studies investigating their correlation, as well as some possible interventional and preventive measures. The critical significance of this study is based on the model that is used to interpret air pollution, which requires geographical data and data from air quality monitoring centers. The model provides reliable output regarding the air quality in a region over a certain period of time. However, estimated glomerular filtration rate (eGFR) based on the serum creatinine levels is the only method of kidney function assessment in this study. Interpretation of structural abnormalities, albuminuria and urinary sediments is also required to prevent misrepresentation of CKD.

An observational cohort study from the USA with more than 2 million participants demonstrated that a 10-$\mu g/m^3$ increase in PM2.5 concentration is linked to a higher risk for eGFR decline of over 30%, eGFR <60 mL/min/1.73 m^2 and CKD over a median follow-up period of 8.5 years [5]. Moreover, air pollution has been linked to an increased need for kidney replacement therapy and mortality in CKD patients [6, 7] (Figure 1). A large-scale meta-analysis of 13 studies that evaluates the association between air pollution and CKD risk, demonstrated a statistically significant increase in CKD risk with an odds ratio (OR) of 1.15 [95% confidence interval (CI): 1.07, 1.24] for each 10 $\mu g/m^3$ increase in PM2.5, 1.25 (95% CI: 1.11, 1.40) for each 10 $\mu g/m^3$

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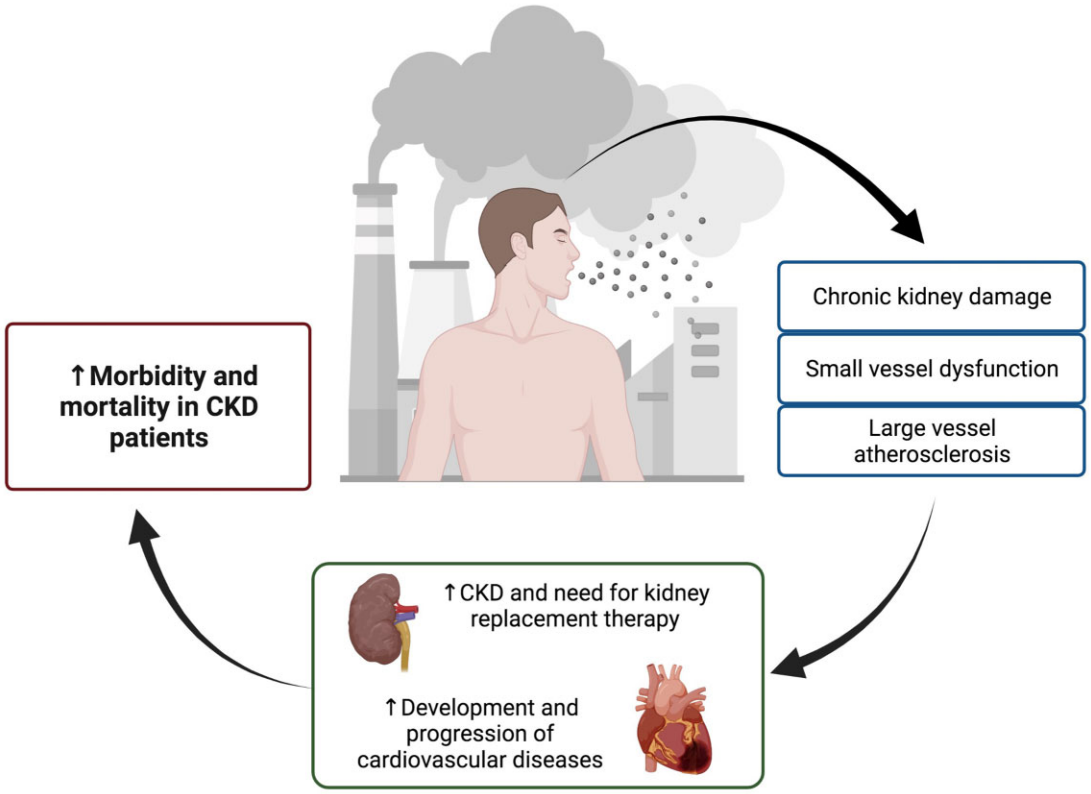

FIGURE 1: Air pollution increases overall mortality and morbidity in CKD patients. Air pollution leads to chronic kidney damage and vascular dysfunction. This accelerates CKD progression and cardiovascular disease.

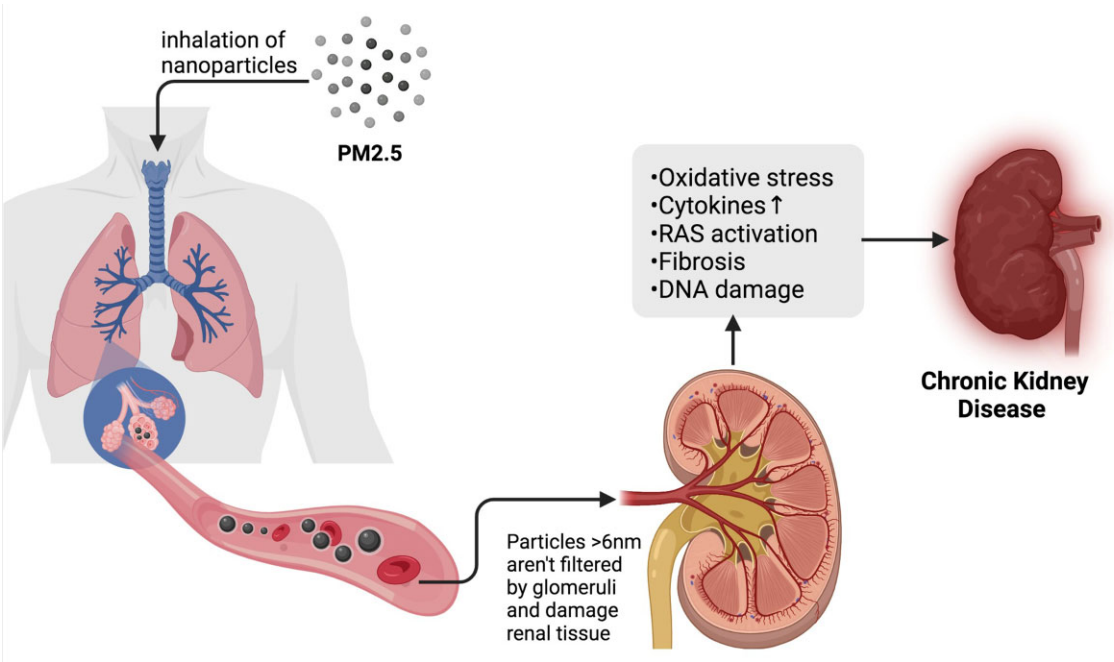

FIGURE 2: The postulated pathophysiology underlying the effect of air pollution on the development of CKD.

increase in PM10. Similar results with weaker associations have been reported with other pollutants such as sulfur dioxide, nitrogen dioxide and carbon monoxide [8]. A study conducted in 2016 revealed that the global burden of incident CKD that is attributable to PM2.5 is 6 950 514 [95% uncertainty interval (UI): 5 061 533–8 914 745] and disability-adjusted life years of CKD attributable to PM2.5 is 11 445 397 (95% UI: 8 380 246–14 554 091) [9]. In addition to the high global disease burden, CKD and its complications that are attributable to air pollution leads to unequal distribution of burden, with an overwhelming predominance in low- and low-to-middle-income countries.

Despite the growing evidence on air pollution and CKD risk, the underlying pathophysiology has yet to be fully understood and hypothetical frameworks are based mostly on animal studies. Approximately 0.2% of the inhaled nanoparticles may reach the renal tissue through systemic circulation, while kidneys are, in most cases, unable to eliminate the particles over 6 nm [10, 11]. Exposure to PM2.5 leads to an elevation of pro-inflammatory cytokines, the imbalance between the oxidants/anti-oxidant molecules, blood pressure elevation, upregulation of the renin-angiotensin-aldosterone system and bradykinin cascade, tissue fibrosis and DNA damage [12–17] (Figure 2). Further studies, especially *in vivo* studies conducted on human tissues, are needed to understand the pathophysiology behind the relationship between air pollution and CKD.

Nevertheless, the study has considerable limitations shared with other geographical studies. It does not consider the individual differences in the use of personal protective equipment, outdoor time spending, seasonal air quality variations and many other potentially harmful air pollutants. Additionally, a selection bias that can underestimate CKD prevalence is present since the study is based on community volunteers. People with better health conditions may potentially be more inclined to participate in this study. However, this study is the first community-based study investigating the association between CKD prevalence and air pollutant levels and thus, has high scientific value. Further community-based studies should assess the impact of preventive measures against air pollution on CKD incidence and progression and on CKD-related global disease burden and mortality.

CONFLICT OF INTEREST STATEMENT

M.K. is a member of the *CKJ* editorial board. The other authors declare no conflict of interest.

(See related article by Lin et al. Long-term exposure to air pollutants and increased risk of chronic kidney disease in a community-based population using a fuzzy logic inference model. *Clin Kidney J* (2022) 15: 1872–1880.)

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