EDITORIAL

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Is ambient air pollution another risk factor of tuberculosis?

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Despite rapid economic development, the prevalence of tuberculosis (TB) is still high in South Korea. The TB prevalence and mortality rates in South Korea are the highest among Organization for Economic Co-operation and Development (OECD) nations [1]. In 2011, there were 50,491 notified TB cases and 2,364 deaths [1].

To control TB, it is important to manage risk factors, which can be classified as factors related to the index case and to the individual. Factors related to the index case include bacillary load and proximity to an infectious case. Other factors are immunosuppressed conditions, such as human immunodeficiency virus coinfection, immune-mediated inflammatory disorders, malnutrition, young age, diabetes, health care worker, socioeconomic and behavioral factors, tobacco smoker, alcohol consumption, indoor air pollution, and demographic factors [2]. With the rapid urbanization and industrialization of South Korea, the level of air pollution has increased. As a result, among the factors related to the individual, studies have focused on environmental factors such as indoor and outdoor air pollution. Air pollution has been identified as a possible risk factor for active TB, and particle exposure with air pollution is associated with an increased risk of human infection [3]. Recent studies of the association between air pollution and TB have examined smoking and biomass fuels. A cross-sectional observational study evaluated the social risk factors for TB in 13,038 patients with TB and reported that smokers developed relatively more pulmonary disease (50%) and more cavitary lesions (90%) and were more likely to require hospitalization, with a longer mean hospital stay, with adjusted odds ratios (aOR) of 1.5, 1.9, and 1.8, respectively [4]. These results corroborate those of other reports suggesting that smoking is responsible for disease severity [5,6]. Another nested case-control study of 255 TB cases and 1,275 controls quantified the association between biomass fuel usage and sputum-positive pulmonary TB. Biomass had a stronger association with pulmonary TB than did smoking, with an odds ratio (OR) of 1.7 and 1.4, respectively [7]. However, a matched case-control study found no association between the use of biomass fuel and the risk of TB in 355 patients with smear-positive pulmonary TB, as compared to 804 age-matched controls. Pulmonary TB was not associated with exposure to biomass fuel smoke, which is contrary to the results of previous studies. One reason might have been because the indoor air pollution (IAP) exposure was similar in

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the TB cases (98.6%) and controls (99.6%), suggesting that IAP exposure is a risk factor for active TB disease [8]. An epidemiological meta-analysis of studies conducted in China suggested that solid-fuel use is more likely to be related to latent TB infection and progression to active TB, with a relative risk (RR) of 1.9 and 1.5, respectively [9]. A prospective case-control study found that TB was strongly associated with household TB exposure (aOR, 25.41; 95% confidence interval [CI], 7.03 to 91.81), household food insecurity (aOR, 11.55; 95% CI, 3.33 to 40.15), and IAP exposure (aOR, 2.67; 95% CI, 1.02 to 6.97) [10]. One recent systematic review and meta-analysis revealed the associations between IAP and TB. Eleven case-control studies and two cross-sectional studies were analyzed to investigate the link between IAP and TB. They found that TB cases were more likely to be exposed to IAP than healthy controls, with a pooled OR of 1.30 [11]. There is limited research on the association of outdoor air pollution and TB. The authors reviewed the medical records of 196 patients diagnosed with culture-positive TB retrospectively and suggested that there was a significant correlation between smear-positive status and residual exposure to particulate matter 2.5 ($PM_{2.5}$). $PM_{2.5}$ might affect TB lung pathology, as evidenced by the link between fine particulate matter levels and smear-positive TB. This study clarifies the correlation of outdoor air pollution with the clinical outcome of TB in our modern age of rapid industrialization and automobile-centric culture. Data indicated that exposure to higher $PM_{2.5}$ levels is significantly associated with smear-positive TB [12]. Ecology studies conducted in countries with high levels of air pollution and pulmonary TB have suggested a link between active disease and ambient air pollution. However, a recent investigation of the concentrations of ambient air pollutants and the rate of pulmonary TB in North Carolina, USA, an area where the air pollution levels are relatively low, reported a potential association between long-term exposure to PM and pulmonary TB disease. The study population included 3,208 pulmonary TB cases with exposure measurements for PM_{10} and 1,853 cases with measurements for $PM_{2.5}$. The only significant association was seen in the adjusted models, and the TB incidence rate ratio was 1.27 (95% CI, 1.30 to 1.60) in the third quintile of $PM_{2.5}$ exposure [13]. In contrast, Hwang et al. [14] reported that concentrations of PM_{10}, O_3, CO, and NO_2 were not associated with the incidence of TB in both males and females. However, the interquartile increase in SO_2 concentration was associated with a 7% increment in TB incidence (RR, 1.07; 95% credible interval [CrI], 1.03 to 1.12) in males but not in females (RR, 1.02; 95% CrI, 0.98 to 1.07) [14].

There are several possible mechanisms explaining the association between air pollution and TB. Particles with diameters < 10 μm, particularly those < 2.5 μm, can penetrate deeply into the lungs and appear to have the greatest potential for adversely affecting health. These pollutants from biomass smoke operate via different mechanisms. Particles < 2.5 μm cause bronchial irritation, inflammation, increased reactivity, reduced mucociliary clearance, reduced macrophage response, and reduced local immunity [15]. Exposure to IAP generates particulate matter, carbon monoxide, nitrous oxides, sulfur oxides, formaldehyde, and benzopyrene [16]. These interfere with mucociliary clearance, induce inflammation, and reduce the antibacterial effects of lung macrophages, which in turn have been implicated in leading to poor lung health [16]. Previous studies linked smoking and indoor or outdoor air pollution with an elevated risk for TB.

The total elimination of particles from the atmospheric environment is impossible. However, a reduction in exposure to prevent particle-related disease, including infection, can be achieved. Recognition of the health risks of particles by both health care workers and the lay public is an important initial step. Smoking cessation will decrease TB. The development of clean energy will reduce the levels of indoor and outdoor air pollutants, which will also decrease infection associated with particle exposure.

In South Korea, the TB burden is still high and air pollution is increasing gradually. Several studies have suggested that air pollution is a risk factor for respiratory infection, especially TB. To eliminate TB in South Korea in the immediate future, it is essential to reduce risk factors, such as air pollution, as well as to manage active TB. In countries were TB is endemic, such as South Korea, a small increase in risk could translate into a large attributable burden. Further studies are needed to understand the burden of TB attributable to air pollution.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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