Science of the Total Environment 631–632 (2018) 47–55

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Ambient air pollutants are associated with newly diagnosed tuberculosis: A time-series study in Chengdu, China

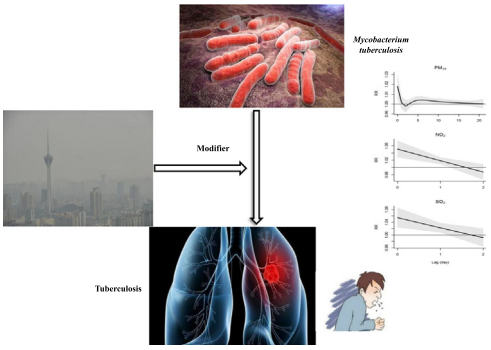
Sui Zhu [a,1], Lan Xia [b,1], Jianlin Wu [b], Shaobing Chen [a], Fei Chen [a], Fangfang Zeng [c], Xiuwei Chen [d], Chuang Chen [b], Yong Xia [b], Xing Zhao [a,*], Juying Zhang [a,*]

[a] Department of Epidemiology and Biostatistics, School of Public Health, Sichuan University, Chengdu 610044, China
[b] Department of Tuberculosis, Sichuan Provincial Center for Disease Control and Prevention, Chengdu 610041, China
[c] Department of Epidemiology, School of Basic Medical Sciences, Jinan University, Guangzhou 510632, China
[d] Department of infectious disease, Sichuan Provincial Center for Disease Control and Prevention, Chengdu 610041, China

HIGHLIGHTS

- It is important to evaluate the associations between ambient air pollutants and incidence of TB in the polluted city.
- Positive associations between PM_{10}, NO_2, SO_2 and the incidence of TB were observed in Chengdu.
- The effect between exposure to PM_{10}, NO_2, and SO_2 and TB cases was not modified by gender or age.
- SO_2 demonstrated remarkable effects in males only.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 22 October 2017
Received in revised form 29 January 2018
Accepted 2 March 2018
Available online xxxx

Editor: SCOTT SHERIDAN

Keywords:
Tuberculosis
Air pollutants
PM_{10}

ABSTRACT

Although a few studies have analyzed the associations between ambient air pollutants and the development of tuberculosis (TB), most have been conducted in the core countries with inconsistent results. In this study, we used a distributed lag non-linear model to investigate the associations between the newly diagnosed TB cases and daily exposure to particulate matter with an aerodynamic diameter of <10 μm (PM_{10}), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) in Chengdu, a severely polluted city. There were 36,108 newly diagnosed active TB cases from January 1, 2010 to December 31, 2015 in Chengdu. In a single-pollutant model, the cumulative relative risk of active TB cases was 1.06 [lag of 0 to 21 days, 95% confidence interval (CI): 1.01–1.11] for each 10 μg/m^3 increase in PM_{10} above the threshold of 70 μg/m^3; 1.06 (lag of 0 to 2 days, 95% CI: 1.03–1.09) for each 10 μg/m^3 increase in NO_2 above the threshold of 40 μg/m^3; and 1.07 (lag of 0 to 2 days, 95% CI: 1.02–1.12) for each 10 μg/m^3 increase in SO_2 above the threshold of 60 μg/m^3. Meanwhile, we found a positive association in males after

Abbreviations: TB, tuberculosis; *M.tb*, *Mycobacterium tuberculosis*; PM, particulate matter; PM_{10}, particulate matter with an aerodynamic diameter of <10 μm; $PM_{2.5}$, Particulate matter with an aerodynamic diameter of <2.5 μm; CO, carbon monoxide; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; CI, confidence interval; PGDP, per capita gross domestic product; NOx, nitrogen dioxides; SCDC, Sichuan Provincial Center for Disease Control and Prevention; PD, population density; MTP, medical technical personnel per 1000 persons; ns, natural cubic spline; df, degrees of freedom; DOW, day of the week; RR, relative risk; QAIC, Akaike information criterion for quasi-likelihood model; ppm, part per million; TNF-α, tumor necrosis factor-α; IFN-γ, interferon-γ; IL, interleukin.

* Corresponding authors at: Department of Epidemiology and Biostatistics, School of Public Health, Sichuan University, No.17 Section 3, Renmin South Road, Sichuan 610044, China.
E-mail addresses: zhaoxing731@gmail.com (X. Zhao), juying109@163.com (J. Zhang).

[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.scitotenv.2018.03.017
0048-9697/

NO_2
SO_2

exposure to a 10 μg/m^3 increase in SO_2 above the threshold of 60 μg/m^3 at a lag of 0 to 2 days. Exposure to PM_{10}, NO_2, and SO_2 was associated with an increment in the incidence of active TB cases.

1. Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* (*M.tb*). In 2016, it was one of the five leading causes of years of life lost, with 1.21 million deaths globally, of which 3.31% (40.12 thousand) occurred in China (Abajobir et al., 2017; Global Burden of Disease Study 2016, 2017). The World Health Organization has reported that nearly one-third of the world's population has latent TB infection (WHO, 2012), and human immunodeficiency virus, malnutrition, alcoholism, smoking, immunosuppressive treatment and diabetes are risk factors for the progression of TB (Ferrara et al., 2012; Kirenga et al., 2015; Lindsay et al., 2014; McDonald et al., 2015).

An ecological study based on historical data observed correlations between coal consumption and TB cases in the United States, Canada, and China, indicating the link between air pollution and TB cases (Tremblay, 2007). A commentary speculated that the outdoor air pollution from combustion sources may be correlated with TB cases (Cohen and Mehta, 2007). An increasing number of studies have explored the link between ambient air pollution and TB cases. Some of these have found associations between particulate matter (PM), especially with an aerodynamic diameter of <10 μm (PM_{10}) and 2.5 μm ($PM_{2.5}$), and TB cases (Jassal et al., 2013; You et al., 2016; Zhang, 2009). In contrast, other studies have found no positive associations between PM and TB cases (Lai et al., 2016; Smith et al., 2014). Ambient carbon monoxide (CO) and nitrogen dioxide (NO_2) are recognized as risk factors of active TB in northern California (Smith et al., 2016) and Taiwan (Lai et al., 2016). Another study conducted in South Korea found that the interquartile increase in sulfur dioxide (SO_2) concentration was associated with a 7% increment in the incidence of TB in males only (Hwang et al., 2014), but no associations were observed for PM_{10}, ozone (O_3), CO, and NO_2. However, a recent study found a negative association between ambient SO_2 concentrations and daily TB patient visits, showing a change of −2.0% [95% confidence interval (CI): −3.2–0.8] with a 10 μg/m^3 increase in SO_2 and a lag of 0–3 days in Ningbo city in China (Ge et al., 2017).

From these previous studies, it is clear that the associations between ambient air pollution and TB cases are inconsistent and that most of the studies were conducted in the core countries. A previous study indicated that TB was generally considered to be linked to industrialization and urbanization (Tremblay, 2007), and TB has mainly been reported to occur in areas with serious air pollution (Sun et al., 2016). Meanwhile, the time-activity patterns, sources, components, and concentration levels of pollution and the population demographic characteristics in the peripheral countries may differ significantly from those in the core countries in ways that may affect human exposure and TB cases. Therefore, more epidemiological studies from peripheral countries, especially those with severe ambient air pollution, are needed to explore the associations. Chengdu, a large city in western China and the capital of Sichuan province, is experiencing an economic boom, with a per capita gross domestic product (PGDP) of 74,273 (yuan) in 2015 (Sichuan Provincial Bureau of Statistics of China, 2016). $PM_{2.5}$ and PM_{10} are the top air pollutants in urban Chengdu (Qiao et al., 2015), while levels of SO_2, O_3, and nitrogen dioxides (NOx) emissions are also high (Ning et al., 2017). Furthermore, the burden of TB is the highest in Chengdu according to the Sichuan Provincial Center for Disease Control and Prevention (SCDC).

As $PM_{2.5}$, O_3, and NOx were not regularly measured until 2013 in Chengdu, we aimed to investigate the associations between daily exposure to PM_{10}, NO_2, and SO_2 and new TB cases. This is the first time-series analysis to explore the association between ambient air pollutants and TB cases in the severely polluted westernmost large city in China.

2. Material and methods

2.1. Study area

Chengdu is located between latitude 30.05°N to 31.26°N and longitude 102.54°E to 104.53°E, and has a total area of 12,119 km^2. At the end of 2015, the population was 14.34 million and the population density (PD) was 1209 (persons/km^2) in all 19 county-level cities (Sichuan Provincial Bureau of Statistics of China, 2016). Located at the bottom of the Sichuan Basin, Chengdu is surrounded by mountains and has a subtropical monsoon climate (Chen and Xie, 2014). The dispersion of locally produced pollutants can be hampered, causing the most severe air pollution in Sichuan province (Ning et al., 2017). According to the China Statistical Yearbook in 2015 (National Bureau of Statistics of China, 2016), the annual PM_{10} concentration was 108 μg/m^3, 1.54 times the level of 70 μg/m^3 recommended by the Chinese National Ambient Air Quality Standards (GB3095-2012) (Ministry of Environmental Protection of the People's Republic of China, 2012).

2.2. TB cases

The primary outcome of this study was newly diagnosed active pulmonary TB in Chengdu. Daily TB case reports were collected from the TB surveillance system and were provided by the SCDC between January 1, 2010 and December 31, 2015. According to the national guidelines on tuberculosis control, pulmonary TB cases or suspected cases detected in any health facilities must be reported through the infectious disease reporting system within 24 h. Confirmed TB cases, based on symptoms, chest X-rays, sputum smears, and mycobacterial culture (Chinese Center for Disease Control and Prevention, 2008), are sent to the TB surveillance system (Wang et al., 2010). Active TB cases can occur soon after initial exposure and infection or after a period of latent TB infection (reactivation disease); clinically however, it is not possible to

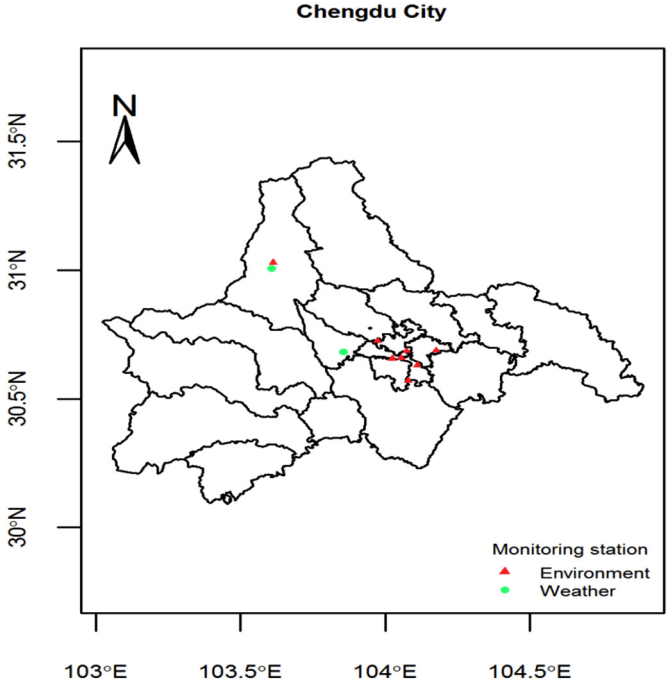


Fig. 1. Locations of environmental and weather monitoring stations in Chengdu.