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Associations between long-term exposure to ambient particulate air pollution and type 2 diabetes prevalence, blood glucose and glycosylated hemoglobin levels in China

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ABSTRACT

Background: The evidence for an association between particulate air pollution and type 2 diabetes mellitus (T2DM) in developing countries was very scarce.
Objective: To investigate the associations of long-term exposure to fine particulate matter ($PM_{2.5}$) with T2DM prevalence and with fasting glucose and glycosylated hemoglobin (HbA1c) levels in China.
Methods: This is a cross-sectional study based on a nation-wide baseline survey of 11,847 adults who participated in the China Health and Retirement Longitudinal Study from June 2011 to March 2012. The average residential exposure to $PM_{2.5}$ for each participant in the same period was estimated using a satellite-based spatial statistical model. We determined the association between $PM_{2.5}$ and T2DM prevalence by multivariable logistic regression models. We also evaluated the association between $PM_{2.5}$ and fasting glucose and HbA1c levels using multivariable linear regression models. Stratification analyses were conducted to explore potential effect modification.
Results: We identified 1760 cases of T2DM, corresponding to 14.9% of the study population. The average $PM_{2.5}$ exposure for all participants was 72.6 μg/m^3 during the study period. An interquartile range increase in $PM_{2.5}$ (41.1 μg/m^3) was significantly associated with increased T2DM prevalence (prevalence ratio, PR = 1.14), and elevated levels of fasting glucose (0.26 mmol/L) and HbA1c (0.08%). The associations of $PM_{2.5}$ with T2DM prevalence and with fasting glucose and HbA1c were stronger in several subgroups.
Conclusions: This nationwide cross-sectional study suggested that long-term exposure to $PM_{2.5}$ might increase the risk of T2DM in China.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a long-term metabolic disorder that is primarily characterized by insulin resistance, relative insulin deficiency, and hyperglycemia. A high fasting blood glucose level was ranked as the 7th risk factor for global disease burden and accounted for 3.4 million deaths (Lim et al., 2012). It was estimated that 590 million people would be suffering from T2DM by the year 2035 (Guariguata et al., 2014). It is also an important risk factor for cardiovascular diseases, leading to enormous health consequences. Furthermore, the development of these outcomes in people with diabetes may be exacerbated by exposure to exogenous toxic factors (Zanobetti and Schwartz, 2001).

There is growing evidence from both human and animal studies suggesting that particulate matter (PM) air pollution is an important risk factor for T2DM (Balti et al., 2014; Esposito et al., 2016; Eze et al., 2015; Liu et al., 2013; Park and Wang, 2014). Dozens of cross-sectional and cohort studies have reported a positive association between long-term exposure to ambient PM and risk for T2DM (Janghorbani et al., 2014; Li et al., 2014; Wang et al., 2014), but some other studies did not find such a relationship. For example, using two large prospective cohorts, the Nurses' Health Study and the Health Professionals Follow-Up Study, Puett et al. failed to find strong evidence of an association between exposure to PM in the previous 12 months and incident diabetes (Puett et al., 2011). Additionally, studies have

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focused on the effects of PM on the incidence, prevalence and mortality of T2DM, but few have explored its effects on glucose homeostatic measures, such as fasting glucose and glycosylated hemoglobin (HbA1c) levels (Rajagopalan and Brook, 2012). HbA1c is a well-acknowledged marker for measuring the average plasma glucose concentration over prolonged periods, and an elevated HbA1c level denotes an increased risk of developing diabetes and its complications (Edelman et al., 2004; Gillett, 2009). Furthermore, most studies on the associations between PM and T2DM were conducted in North America and Europe, and the evidence has been very limited in developing countries, where a steep increase in T2DM was observed in the past few decades and where the air pollution level is much higher (Nicole, 2015).

As the largest developing country, China is facing a growing prevalence of diabetes and severe air pollution problems (Yang et al., 2013). Given the vast population affected by diabetes and the ubiquitous exposure to air pollution, it is of increasing public health significance to examine the impacts of PM on diabetes. Therefore, the objective of this study was to evaluate the association of long-term exposure to PM with T2DM and with fasting blood glucose and HbA1c levels in China. This study was based on a nationally representative survey of the China Health and Retirement Longitudinal Study (CHARLS) project (Zhao et al., 2014), which aimed to provide a high-quality public database with a wide range of information to facilitate needs of scientific and policy research on ageing-related issues.

2. Materials and methods

2.1. Study population and health data

This is a cross-sectional study based on a national baseline survey within the CHARLS project. This baseline survey was conducted from June 2011 to March 2012 and included 17,708 middle-aged and elderly participants (≥45 years old) (Zhao et al., 2014). Briefly, these participants were selected from 150 counties or districts from 28 provinces using a four-staged, stratified and cluster sampling method. Individual information on sociodemographic characteristics, behaviors, indoor air pollution and chronic diseases (T2DM, etc.) was obtained using a standardized questionnaire. Sociodemographic information included home address, location of residence (rural or urban according to China's administrative divisions), age, sex, education level (low, ≤5 years; medium, 6–9 years; high, ≥10 years) and body mass index (BMI). Behavioral variables included smoking status (current; former: quitted smoking ≥3 years; never), pack years of smoking (packs per day multiplied by the years of smoking) and alcohol drinking (>1/month; <1/month; none). Indoor air pollution levels were represented by the type of energy used for heating (central heating; clean; unclean; others) and cooking (clean; unclean; others). The response rate of the survey was 80.5%. The reasons for nonresponse included recusal (8.8%), loss of contact (8.2%) and others (2.5%).

A blood test was conducted to measure the fasting glucose and HbA1c levels of participants who were willing to donate venous blood samples. Blood bioassays were performed at the Youanmen Center for Clinical Laboratory of Capital Medical University. HbA1c levels were measured using the Boronate affinity HPLC method, with a variation coefficient of 1.90% within assays and 2.10% between assays. Glucose levels were tested using an enzymatic colorimetric method with a variation coefficient of 0.90% within assays and 1.80% between assays. In total, 92% of the subjects claimed to have fasted overnight and non-fasting samples were excluded from this analysis.

A total of 5861 individuals in the nationwide survey were excluded from this analysis due to the refusal to blood donation; thus, we finally included 11,847 participants. The main definition of T2DM was self-reported diabetes, and/or fasting glucose ≥7 mmol/L, and/or HbA1c ≥ 6.5%, and/or insulin use according to the recommendations of the American Diabetes Association (American Diabetes Association, 2014; Eze et al., 2014; Yuan et al., 2015). To ensure that the calculations would be representative of the overall Chinese population aged 45 years or older, weights were used to correct for household non-response in the initial sampling and separately for individual non-response in the blood sampling. In brief, corrections for non-response were created using a propensity score from a logit regression of the household being measured or the individual giving blood on numerous covariates. We then took the inverse probability for each observation and multiplied that by the regular sample weight (Zhao et al., 2016).

2.2. Air pollution data

The geocoded residential addresses of 11,847 participants were linked to average $PM_{2.5}$ concentrations between June 2011 and March 2012, which were estimated from a satellite-based spatial statistical model developed by Ma et al. (2015). Briefly, this model was established using the Collection 6 aerosol optical depth (AOD) retrieved by the US National Aeronautics and Space Administration (NASA) Moderate Resolution Imaging Spectroradiometer (MODIS), assimilated meteorology data, land use data (fire spots, urban and forest cover, etc.) and $PM_{2.5}$ concentrations from China's ground monitoring network, which was established at the end of 2012. This model was validated to have little bias in the monthly and seasonal estimates on $PM_{2.5}$. For a certain grid cell, the model could not predict the $PM_{2.5}$ value if the AOD value was missing. A minimum of 6 data points of AOD in a month was shown to be sufficient to appropriately represent a monthly average (Ma et al., 2015). To allow for the adjustment for atmospheric ozone (O_3), we obtained the O_3 exposure data during the study period from the database of the 2013 Global Burden of Disease (GBD) project, which was estimated using the global chemical transport model TM5 (Brauer et al., 2015).

The geocoding and exposure assignment was conducted in ArcMap (Version 10.2). Specifically, we merged the grid cells of modeled data over the study period with the boundaries of China's administrative divisions. Each grid cell had a spatial resolution of 10 km × 10 km, with individuals who resided in the same cell sharing the same exposure levels. The modeled exposures were recorded as monthly averages, and we calculated the average concentrations during our study period (June 2011 to March 2012) as indicators of the historical (long-term) exposure, assuming that the annual exposure varied little in recent years. For sensitivity analysis, we obtained another source of modeled $PM_{2.5}$ concentrations from the GBD database, which generated yearly average estimates by combining the satellite-based estimates, chemical transport model (TM5) simulations and ground measurements (Brauer et al., 2015).

2.3. Statistical analysis

We evaluated the long-term associations of exposure to $PM_{2.5}$ with T2DM prevalence and glucose homeostatic measures (*i.e.*, fasting glucose and HbA1c levels) using the crude (rather than weighted) data. For T2DM prevalence, we calculated odd ratios associated with an interquartile range (IQR) increase in $PM_{2.5}$ using multivariable logistic regression models. The odds ratio might overstate the relative risk in cross-sectional studies; thus, we further calculated the prevalence ratios (PRs) of T2DM using the formula $PR = OR / ((1 - P_0) + (P_0 \times OR))$ (Zhang and Yu, 1998), in which P_0 was the crude prevalence of T2DM in this analysis. For glucose homeostatic measures, we calculated changes in fasting glucose and HbA1c levels associated with an IQR increase in $PM_{2.5}$ using multivariable linear regression models.

We established a crude model and an adjusted model. Specifically, the crude model referred to the unadjusted analysis and crude effects were estimated. In the adjusted model, we controlled for sociodemographic characteristics (age, sex, BMI, educational level and location of residence), behavioral variable (smoking, drinking and indoor air pollution) and ambient O_3 as potential confounders according