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Ambient particulate matter associates with asthma in high altitude region: A population-based study

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ABSTRACT

Background: Exposure to particulate matter (PM) has been a major public health threat, but the potentially differential effects on asthma of PM remain largely unknown in high altitude settings. We evaluated the effects of ambient PM on asthma in high altitude settings.

Methods: The study recruited a representative sample from high altitude settings using a multistage stratified sampling procedure. Asthma was defined by a self-reported history of diagnosis by a physician or by wheezing symptoms in the preceding 12 months. The annual mean $PM_{2.5}$ and PM_{10} concentrations were calculated for each grid cell at 1-km spatial resolution based on the geographical coordinates.

Results: We analyzed data for participants (mean age 39.1 years, 51.4% female) and 183 (3.7%, 95% confidence interval (CI): 3.2–4.2) of the participants had asthma. Prevalence was higher in women (4.3%, 95% CI 3.5–5.1) than in men (3.1%, 2.4–3.8) and increasing with higher concentration of PM exposures. For an interquartile range (IQR) difference (8.77 $\mu g/m^3$) in $PM_{2.5}$ exposure, the adjusted odds ratio (OR) was 1.64 (95% CI 1.46–1.83, $P < 0.001$) for risk of asthma. For PM_{10}, there was evidence for an association with risk of asthma (OR 2.34, 95% CI: 1.75–3.15, $P < 0.001$ per IQR of 43.26 $\mu g/m^3$). Further analyses showed that household mold or damp exposure may aggravate PM exposure associated risks of asthma.

Conclusions: This study identified that PM exposure could be a dominate environmental risk factor for asthma but largely unconsidered in the high-altitude areas. The association between PM exposure and asthma should be of interest for planners of national policies and encourage programs for prevention of asthma in residents living at high altitudes.

Keywords: Asthma, Air pollution, High altitude, Particulate matter, Low- and middle-income region

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INTRODUCTION

Asthma is one of the major chronic airway diseases around the world characterized by higher morbidity, mortality, and economic costs.[1,2] Globally, asthma affects 262.4 million people as estimated in 2019, with low- and middle-income countries (LMICs) contributing 96% of global asthma-related deaths,[3] and 495.1 hundred deaths from asthma were estimated and 22.8 million disability-adjusted life-years (DALYs) in 2017.[4,5] Due to social and economic development, accelerated urbanization, environment, and lifestyle changes as well as population aging, the prevalence of asthma is increasing rapidly worldwide particularly in LMICs. There was limited research on asthma at high altitude.[6-8] However, most of these studies included just subjects younger than 20 years of age and paid little attention to the effect of particulate matter on asthma. In addition to well known risk factors such as obesity and allergic rhinitis, a variety of allergens and air pollution, especially particulate matter (PM), were associated with management of asthma.[9-11]

Exposure to PM activates the lung oxidative stress and interacts with different components of the immune system and ultimately enhances allergic inflammatory response. Particularly, fine particulate matter defined by an aerodynamic diameter $\leq$2.5 μm ($PM_{2.5}$) can reach the terminal bronchioles and alveolar region which can cause new cases of asthma and exacerbate pre-existing asthma.[12] Several population-based studies have manifested a significant relationship between PM and asthma.[13,14] The effects of PM exposure on asthma include contributions to asthma development,[15-18] associations with increased risk of asthma symptoms,[19] and asthma lung function deficits.[20-22] However, limited evidence exists regarding the effects of PM on asthma among low- and middle-income residents, particularly in high altitude areas.

In this study, we aimed to depict the overall characteristics, environmental exposures, chronic respiratory symptoms, and pulmonary function parameters of people living at high altitude. We also determined the prevalence of asthma, estimated the risk factors for prevalent asthma, and quantified the association between PM exposure and asthma among residents living in high altitude in China in this population-based study.

METHODS

Study design and participants

The study was performed in the region with altitude of 2100–4700 m and selected a representative sample of subjects through a multistage stratified sampling procedure which covering geographical region, degree of urbanization, and the sex and age distribution during June 2015 and August 2016. Details of the design and sampling method of the study have been presented previously.[23] Shortly, we firstly selected 8 districts or counties in both urban (2 districts) and rural (6 counties) areas by the probability proportional to size method. Then 2 streets or townships were picked out from each district or county, and 3 communities or village communities were picked out from each street or township by a simple random sampling method. Finally, according to the 2010 China census data from communities or villages, we chose participants from each of the sex/age strata through the same method. Only 1 participant from each household was chosen. The permanent residents (ie, living in their current residence for more than 1 year) aged $\geq$15 years were included for the analysis. The excluded criteria were treatment for tuberculosis during the study, hospital admission for any cardiac condition in the preceding 3 months, any condition that would interfere with spirometry (such as recent thoracic, abdominal, or eye surgery, or retinal detachment), and women who were pregnant or breastfeeding.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Procedures

Pulmonary function tests were performed in all qualified study participants (spirometry) through a MasterScreenTM Pneumo PC spirometer (CareFusion, Yorba Linda, CA) according to American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations by trained technicians.[24,25] Each participant was required to do the same procedure twice, before and after receiving a bronchodilator (400 µg of salbutamol through a 500 ml spacer). The expert panel of physicians and senior technicians in local health centres were responsible for the checking of measurement results on the basis of criteria from the ATSociety/ERS criteria to perform strictly quality control. A standardized questionnaire covering demographic characteristics, clinical measurements, medical history, history of related respiratory disease, smoking status, living conditions, respiratory symptoms, and occupational and environmental factors was administered by experienced interviewers at local community centers.

Asthma and particulate matter exposure

Asthma was determined by a self-reported history of asthma diagnosis by a physician or by wheeze symptoms in the preceding 12 months based on the asthma questionnaire from the European Community Respiratory Health Survey (ECRHS).[26] This questionnaire has been well validated by the national cross-sectional study in China.[27]

$PM_{2.5}$ concentrations were predicted by random forest models at daily level and 1 km × 1 km spatial resolution in 2013–2019 in mainland China with full spatiotemporal coverage. The detailed methodology was described in the previous study[28] and summarized here. Random forest models were developed with ground measured $PM_{2.5}$ concentrations as a dependent variable, and Multi-Angle Implementation of Atmospheric Correction aerosol optical depth (MAIAC AOD), MERRA-2 simulated $PM_{2.5}$ concentrations, meteorological parameters, land use data, and population density as predictor variables in 2013–2019. Overall, ten-fold cross validation R^2 and root-mean-square error (RMSE) values between measured and predicted $PM_{2.5}$ at daily level of the random forest models were 0.84 and 16.08 µg/m^3, respectively. PM_{10} concentrations were predicted by random forest models at daily level and 1 km × 1 km spatial resolution in 2013–2019 in mainland China with full spatiotemporal coverage. We developed random forest models by combining ground measured PM_{10} concentrations, Multi-Angle Implementation of Atmospheric Correction aerosol optical depth (MAIAC AOD), MERRA-2 simulated PM_{10} concentrations, PM_{10} simulations from the Community Multiscale Air Quality (CMAQ) modeling system, meteorological parameters, land use data, visibility, and population density. Overall, ten-fold cross validation R^2 and root-mean-square error (RMSE) values between measured and predicted PM_{10} at daily level of the random forest models were 0.86 and 23.15 µg/m^3, respectively.

The monthly and annual mean $PM_{2.5}$ and PM_{10} concentrations were calculated for each grid cell at 1-km spatial resolution. They were assigned to participants based on the geographical coordinates, which were converted by the specific address information through geocoding, respectively.

Variables

Small airway dysfunction was diagnosed when at least 2 of the following 3 indicators were less than 65% of predicted values: MMEF, FEF at 50% of vital capacity, and FEF at 75% of vital capacity.[29] Allergic rhinitis was defined based on the Allergic Rhinitis and Its Impact on Asthma (ARIA) questionnaire.[30]

Statistical analysis

The analyses included a description of the sample, evaluation of mean spirometric results, and calculation of the prevalence of asthma. The Analysis of Variance (ANOVA) or Student's *t*-test for continuous variables and by $\chi 2$ test for categorical variables were tested. Multivariable logistic regression models were built to quantify the relationship between PM exposures and asthma. The models also included odds ratios (ORs) with 95% confidence intervals (CIs). Difference of lung function parameters, including the means and 95% CIs, per interquartile range (IQR) change of $PM_{2.5}$ or PM_{10} were statistically analyzed by multivariable linear regression models. Potential confounders considered were: age, gender, body mass index (BMI), educational level, smoking status, household mold or dampness, and allergic rhinitis. The statistically significant differences were considered with two-sided $p < 0.05$. In addition, we conducted several subgroup analyses stratified by the above variables and further assessed the potential interaction by using a multiplicative interaction term between PM exposure and a categorization variable. Associations were estimated by ORs and

	Total (n = 4967)	Male (n = 2415)	Female (n = 2552)	P value
Age, years	39.10 (14.33)	37.89 (14.30)	40.25 (14.26)	<0.001
15-44	3248 (65.4%)	1679 (69.5%)	1569 (61.5%)	<0.001
45-64	1471 (29.6%)	614 (25.4%)	857 (33.6%)	
≥65	248 (5.0%)	122 (5.1%)	126 (4.9%)	
Education attainment				
Primary school and lower	2668 (53.7%)	1048 (43.4%)	1620 (63.5%)	<0.001
Middle and high school	1326 (26.7%)	747 (30.9%)	579 (22.7%)	
College and higher	973 (19.6%)	620 (25.7%)	353 (13.8%)	
BMI, kg/m^2	23.72 (3.99)	23.61 (3.72%)	23.82 (4.23%)	0.076
<18.5	361 (7.3%)	160 (6.6%)	201 (7.9%)	0.197
18.5–24.9	2880 (58.0%)	1420 (58.8%)	1460 (57.2%)	
≥25.0	1726 (34.7%)	835 (34.6%)	891 (34.9%)	
Cigarette smoking				
Never-smoker	3604 (72.6%)	1233 (51.1%)	2371 (92.9%)	<0.001
Ever-smoker	1363 (27.4%)	1182 (48.9%)	181 (7.1%)	
Household mold or damp	175 (3.7%)	76 (3.3%)	99 (4.1%)	0.175
PM2.5 exposure, ug/m^3	33.57 (10.78)	33.30 (10.98)	33.82 (10.58)	0.088
<26	2060 (41.5%)	1112 (46.0%)	948 (37.1%)	<0.001
26-34	1716 (34.5%)	745 (30.8%)	971 (38.0%)	
≥35	1191 (24.0%)	558 (23.1%)	633 (24.8%)	
PM10 exposure, ug/m^3	66.73 (23.47)	64.99 (23.54)	68.37 (23.28)	<0.001
<48	1393 (28.0%)	834 (34.5%)	559 (21.9%)	<0.001
48–90	2309 (46.5%)	994 (41.2%)	1315 (51.5%)	
≥91	1265 (25.5%)	587 (24.3%)	678 (26.6%)	
Symptoms				
Frequent cough	712 (14.6%)	365 (15.3%)	347 (13.9%)	0.167
Sputum	656 (13.4%)	397 (16.7%)	259 (10.4%)	<0.001
Recurrent wheezing	257 (5.3%)	106 (4.5%)	151 (6.0%)	0.015
Dyspnea in daily life	1403 (28.7%)	591 (24.8%)	812 (32.5%)	<0.001
Lung function parameters				
FVC post-BD, L	3.78 (0.99)	4.30 (0.96)	3.28 (0.72)	<0.001
FVC post-BD % pred	106.71 (24.75)	101.17 (21.24)	111.94 (26.62)	<0.001
FEV1 post-BD, L	3.17 (0.86)	3.61 (0.85)	2.77 (0.64)	<0.001
FEV1 post-BD % pred	106.21 (25.63)	101.85 (21.72)	110.33 (28.25)	<0.001
FEV1/FVC post-BD, %	84.44 (9.77)	84.20 (10.11)	84.66 (9.43)	0.098
MMEF post-BD, L	3.20 (1.38)	3.58 (1.48)	2.83 (1.17)	<0.001
MMEF post-BD % pred	83.30 (33.87)	84.55 (33.55)	82.10 (34.14)	0.014
FEF50% post-BD, L	4.22 (1.58)	4.77 (1.70)	3.70 (1.25)	<0.001
FEF50% post-BD % pred	95.30 (31.69)	98.12 (32.34)	92.63 (30.83)	<0.001
FEF75% post-BD, L	1.93 (1.01)	2.15 (1.12)	1.72 (0.83)	<0.001
FEF75% post-BD % pred	102.49 (52.64)	104.85 (52.50)	100.27 (52.69)	0.003
Asthma	183 (3.7)	74 (3.1)	109 (4.3%)	0.029
SAD	1417 (28.8%)	614 (25.7%)	803 (31.8%)	<0.001
Allergic rhinitis	711 (14.5%)	291 (12.2%)	420 (16.8%)	<0.001

Table 1. Demographics and risk factors by gender in the high-altitude residents. *Data are expressed as number (%) or mean (standard deviation, SD). BMI, Body mass index; $PM_{2.5}$, Particulate matter with a diameter ≤2.5 μm; PM_{10}, Particulate matter with a diameter ≤10 μm; post-BD, post-bronchodilator; FVC, Forced vital capacity; FEV_1, Forced expiratory volume in the first second; MMEF, Maximum mid-expiratory flow; FEF, Forced expiratory flow; SAD, Small airway dysfunction*

	Overall %, 95%CI	Men %, 95%CI	Women %, 95%CI
Prevalence	3.7 (3.2–4.2%)	3.1 (2.4–3.8%)	4.3 (3.5–5.1%)
Age, years			
15-44	2.0 (1.5–2.5%)	1.4 (0.9–2.1%)	2.5 (1.8–3.5%)
45-64	5.6 (4.5–6.9%)	4.9 (3.3–6.9%)	6.2 (4.7–8.0%)
≥65	14.5 (10.4–19.5%)	16.4 (10.3–24.2%)	12.7 (7.4–19.8%)
P for difference	<0.001	<0.001	<0.001
Education attainment			
Primary school and lower	5.0 (4.2–5.9%)	4.8 (3.6–6.2%)	5.2 (4.2–6.4%)
Middle and high school	2.6 (1.8–3.7%)	2.4 (1.4–3.8%)	2.9 (1.7–4.7%)
College and higher	1.4 (0.8–2.4%)	1.0 (0.4–2.1%)	2.3 (1.0–4.4%)
P for trend	<0.001	<0.001	0.009
BMI, kg/m^2			
<18.5	3.3 (1.7–5.7%)	2.5 (0.7–6.3%)	4.0 (1.7–7.7%)
18.5–24.9	2.7 (2.1–3.3%)	2.0 (1.4–2.9%)	3.3 (2.4–4.3%)
≥25.0	5.4 (4.4–6.6%)	4.9 (3.5–6.6%)	5.9 (4.5–7.7%)
P for trend	<0.001	<0.001	0.008
Cigarette smoking			
Never-smoker	3.4 (2.8–4.1%)	2.6 (1.8–3.6%)	3.8 (3.1–4.7%)
Ever-smoker	4.4 (3.4–5.6%)	3.6 (2.6–4.8%)	9.9 (6.0–15.3%)
P for difference	0.098	0.172	<0.001
Household mold or damp			
Yes	10.9 (6.7–16.4%)	5.3 (1.5–12.9%)	15.2 (8.7–23.8%)
No	3.6 (3.1–4.2%)	3.2 (2.5–4.0%)	4.0 (3.3–4.9%)
P for difference	<0.001	0.310	<0.001
Small airway dysfunction			
Yes	6.5 (5.3–7.9%)	5.0 (3.5–7.1%)	7.6 (5.9–9.7%)
No	2.5 (2.0–3.1%)	2.4 (1.7–3.2%)	2.7 (2.0–3.6%)
P for difference	<0.001	<0.001	<0.001
Allergic rhinitis			
Yes	7.0 (5.3–9.2%)	7.2 (4.5–10.8%)	6.9 (4.7–9.8%)
No	3.2 (2.7–3.8%)	2.5 (1.9–3.3%)	3.8 (3.1–4.8%)
P for difference	<0.001	<0.001	0.004

Table 2. The prevalence of asthma in the residents aged 15 years older living at high altitude. *CI, Confidence interval; BMI, body mass index; $PM_{2.5}$, Particulate matter with a diameter ≤2.5 μm; PM_{10}, Particulate matter with a diameter ≤10 μm.**Data missing for household mold or damp (n = 281), small airway dysfunction (n = 55), allergic rhinitis (n = 75)*

their 95% CIs, associated with per IQR increase in PM exposures. Additionally, we used a natural cubic spline term with 3° of freedom for $PM_{2.5}$ and PM_{10} to model dose-response curves. All analyses were performed with R statistical program version 4.0.3 (www.r-project.org/).

RESULTS

As shown in Figure S1, 5843 subjects were participated in the survey; 196 refused to join in the survey, and 680 were excluded from the analysis because they were unable to finish the

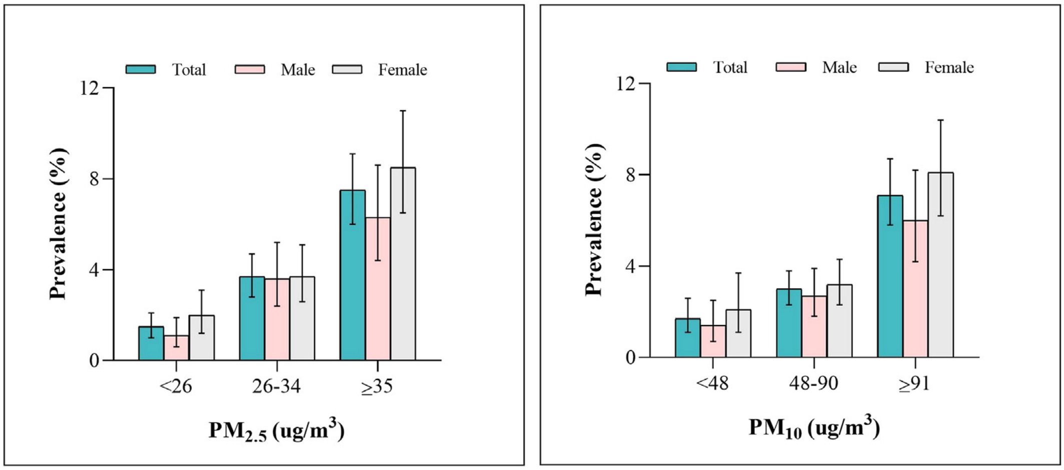

Fig. 1 The prevalence of asthma based on PM exposures in population aged 15 years and older. A. The prevalence of asthma for subjects exposed to different subgroups of $PM_{2.5}$ based on sex. B. The prevalence of asthma for subjects exposed to different subgroups of PM10 based on sex. Bars represent mean prevalence and error bars represent 95% CI.

spirometry examination, had failed to complete the post-bronchodilator test, or had unreliable results from the post-bronchodilator test. Finally, the analysis for asthma included 4967 individuals (2415 men and 2552 women) who finished the questionnaire survey and had credible pulmonary function tests before and after using a bronchodilator.

Data descriptive statistics

Table 1 summarizes the general characteristics and risk factors of the study population. Among the 4967 participants, 183 (3.7%) had diagnosed with asthma and 1417 (28.8%) had small airway dysfunction. The average concentration of $PM_{2.5}$ and PM_{10} was 33.57 (10.78) ug/m^3 and 66.73 (23.47) ug/m^3, respectively. The characteristics and risk factors of the study population grouped according to IQR of $PM_{2.5}$ and PM_{10} are presented in Table S1 and S2. Subjects exposed to highest concentration of $PM_{2.5}$ ($\geq$35 μg/m^3) and PM_{10} ($\geq$91 μg/m^3) tended to have a higher proportion of exposure mold or damp, a higher proportion of asthma and small airway dysfunction.

The prevalence of asthma

The overall prevalence of asthma was 3.7% (95% CI 3.2–4.2) among the general population aged 15 years or older (Table 2). Women had a higher prevalence (4.3%, 95% CI 3.5–5.1%)) than did men (3.1% 95% CI 2.4-3.8; $p < 0.001$). This sex difference was noted among age groups in the general population. The prevalence increased with age and was 2.0% (95% CI 1.5–2.5) among individuals aged 15–44 years, 5.6% (4.5–6.9) among those aged 44–45 years, and 14.5% (10.4–19.5) among those aged 65 years or older in the general population ($p < 0.001$ for age difference). Besides that, the prevalence of asthma increased with increase of concentrations based on subgroups of $PM_{2.5}$ and PM_{10} (Fig. 1). Asthma prevalence was higher in residents exposed to 35 μg/m^3 or higher concentration of $PM_{2.5}$ (7.5%, 95% CI 6.0–9.1) than 26–34 μg/m^3 (3.7%, 95% CI 2.8–4.7) and lower than 26 μg/m^3 (1.5%, 95% CI 1.0–2.1). In the subgroups of PM_{10}, asthma prevalence was 7.1% (95% CI 5.8–8.7) for 91 μg/m^3 or higher, 3.0% (2.3–3.8) for 48–90 μg/m^3 and 1.7% (1.1–2.6) for lower than 48 μg/m^3.

Associations by particulate matter exposures

Table 3 outlines associations of PM exposures with asthma. PM exposures were closely related with increased risk of asthma. After controlling for gender, age, BMI, education, smoking status, exposure to household mold or dampness, and allergic rhinitis, the OR (95% CI) were 1.64 (1.46–1.83) for asthma associated with each IQR rise in $PM_{2.5}$ concentration (8.77 μg/m^3) and 2.34 (1.75–3.15) for asthma associated with each IQR rise in PM_{10} concentration (43.26 μg/m^3). The exposure-response curves between PM exposures and asthma suggested an approximately linear relationship (Fig. 2).

Exposures	Asthma	
	OR (95% CI)	*P* value
$PM_{2.5}$ (per 8.77 μg/m^3 increase)		
Crude OR (95% CI)	1.60 (1.44–1.76)	<0.001
Adjusted OR (95% CI)[a]	1.64 (1.46–1.83)	<0.001
PM_{10} (per 43.26 μg/m^3 increase)		
Crude OR (95% CI)	2.50 (1.91–3.29)	<0.001
Adjusted OR (95% CI)[a]	2.34 (1.75–3.15)	<0.001

Table 3. Estimates of ORs for asthma associated with per interquartile range increase exposure to PM. *$PM_{2.5}$, Particulate matter with a diameter ≤2.5 μm; PM_{10}, Particulate matter with a diameter ≤10 μm; OR, odds ratio; CI, confidence interval. [a]Adjusted OR: adjustments for age, sex, BMI, education, smoking status, exposure to household mold or damp, and allergic rhinitis*

Figure S2 and Figure S3 elucidate subgroup analyses of PM exposures and asthma associations stratified by gender, age group, education level, BMI, allergy rhinitis, and environmental factors (ie, smoke status and household mold or damp). We observed suggestive evidence that household mold or dampness exposure may aggravate $PM_{2.5}$ associated risks of asthma, with P value of 0.034 for the interaction of household mold or dampness exposure with $PM_{2.5}$, but we failed to identify any significant modifying effects with PM_{10}.

Associations of particulate matter exposures with lung function

For asthma population, there were statistically significant and inverse associations of PM exposures with some indicators of lung function. Table S3 and S4 revealed the estimates on volume and flow indicators of lung function associated with per IQR increase of PM exposures. $PM_{2.5}$ was statistically significantly associated with lower measurements of FEV_1, $FEF_{50\%}$ and $FEF_{75\%}$. An IQR increase of $PM_{2.5}$ concentrations was associated with lower FEV_1 (96.80 ml, 95% CI: 26.68–166.96), $FEF_{50\%}$ (197.58 ml, 95% CI: 63.99-331.17) and $FEF_{75\%}$ (170.29 ml, 95% CI: 97.42–243.16). For lung function parameters, there was no statistically significant association was found with PM_{10}.

DISCUSSION

To our knowledge, the population-based study has provided the prevalence and related risk factors of asthma among residents aged 15 years or older living in high altitude. Our large comprehensive asthma survey, which through a stringent sampling design and standard methods for asthma assessment, found an asthma prevalence of 3.7% among the high-altitude residents. After adjustment for confounding factors, PM exposures was associated with an increased odds of asthma which could be aggravated by household mold or damp exposure.

Asthma has been identified as the most prevalent chronic respiratory disease worldwide by the Global Burden of Disease study. A study from 70 countries determined that the global prevalence of wheezing in adults aged 18–45 years was estimated to be 4.3% (95% CI: 4.2–4.4), with the highest rates found in Australia (27.4%), the Netherlands (22.7%), the United Kingdom (22.6%), Brazil (22.6%), and Sweden (21.6%).[31] The prevalence of asthma in China is likely to increase rapidly due to accelerated urbanization, ageing population and fast changes in the environment. Below 1500 m areas in China, the prevalence of physician diagnosed asthma was 1.2%[32] and the prevalence of asthma range from 4.2% to 5.8%[27,33] on the basis of wheezing and physician diagnosis. However, very limited specific data exist concerning prevalence of asthma in high altitudes.

There are a few prior studies on prevalence of asthma at high altitude. A study in urban Lhasa characterized schoolchildren aged 13–14 years and found that the overall prevalence was 3.3%, based on diagnosed to have asthma, having ever

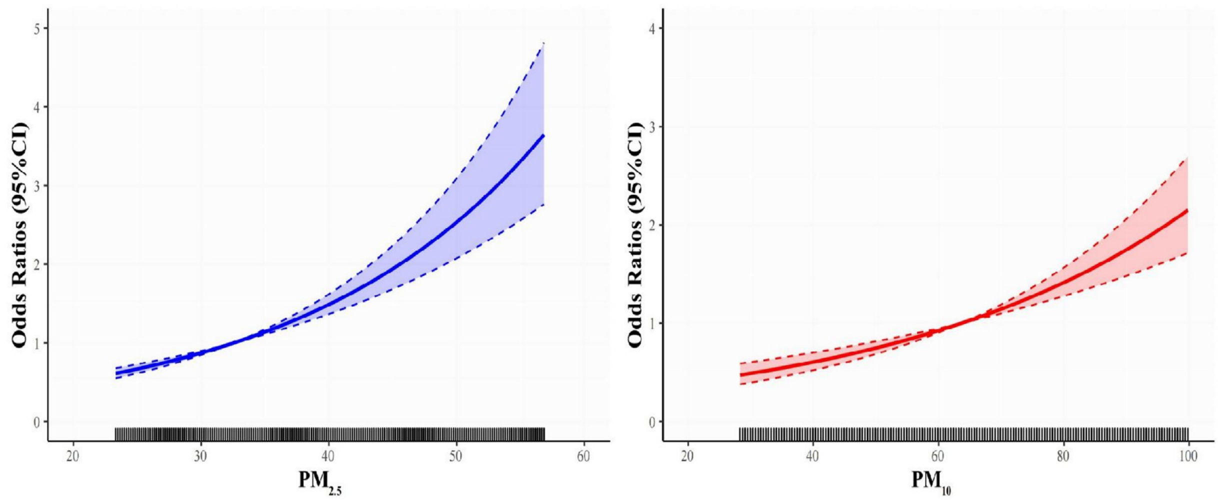

Fig. 2 Concentration response curves between PM exposures and asthma. A. $PM_{2.5}$ exposures associate with the risk of asthma. B. PM_{10} exposures associate with the risk of asthma.

experienced wheezing, and current wheezing.[6] This result was similar to our findings of asthma prevalence. According to a study by Chelsea Gaviola et al, who analyzed 509 participants from urban and rural Puno (3825 m elevation Highly), the estimated prevalence of asthma was 4.0% for urban subjects and 1.8% for rural subjects, respectively.[7] A cross-sectional, multi-centre survey from GAN Phase I carried out in 15 centres corresponding to 14 Mexican cities throughout 2016–2019 found wheezing ever prevalence was 26.2% (95% CI 25.8–26.7%) in school children and 23.9% (95% CI 23.4–24.3%) in adolescents, and there was a negative relation with center sea level altitude higher than 1500 m above mean sea level ($p < 0.005$).[8] However, these studies included just adolescents and used a relatively small sample or lack of rigorous random sampling methods. More importantly, these studies did not explore the relationship between particulate matter exposure and asthma. Ultimately, by using a standard method for asthma definition, we detected the asthma prevalence with higher sensitivity, which is important in low- and middle-income countries where medical resources and equipment were scarce for accurate diagnosis.

Previous studies found that PM exposure had an approximate linear relationship with asthma and was positively associated with an increase in odds of asthma. Our results are generally consistent with several previous studies.[13,16,17,34] A cohort study using data of 3687 participants showed higher incidence of asthma until the age of 20 years with higher exposure to pollutants at the birth address (OR [95% CI]: 1.09 [1.01–1.18] for PM_{10} per IQR increase) that were rather persistent with age.[15] Another cohort study in Toronto, Canada found that long-term $PM_{2.5}$ exposure could contribute to increases in the incidence of adult asthma independent of other potential risk factors.[17] One study from 2008 to 2013 Survey of the Health of Wisconsin (SHOW) program found that an increase of 5 $\mu g/m^3$ in the annual mean $PM_{2.5}$ can lead to a 3.58 increase in the adjusted odds of having asthma.[34] Another large national cohort study performed among American women reported that higher $PM_{2.5}$ concentrations were associated with incident wheeze and asthma.[16] And the cross-sectional study in 6 low- and middle-income countries found that the adjusted prevalence ratio of asthma was 1.05 for each 10 $\mu g/m^3$ increase in $PM_{2.5}$ after controlling for the effects other confounders, suggesting that long-term exposure to $PM_{2.5}$ might be an important risk factor of asthma.[13] The SAPALDIA cohort study investigating associations between traffic-related particulate matter up to 10 mm in diameter (TPM_{10}) and the incidence of asthma found that the hazard ratio (1.30; 95% CI 1.05 to 1.61) per 1 mg/m^3 change in TPM_{10}.[18] Besides, we found that some indicators of lung function were significantly inverse associations of $PM_{2.5}$ among asthma cases. The results were consistent with the prior studies. A longitudinal panel study in

Beijing by Ruirui Duan et al found that lower FEV_1, FVC, and PEF was associated with $PM_{2.5}$ exposure in asthma patients.[22] Another large-scale study among Chinese populations also confirmed that exposure to ambient $PM_{2.5}$ was associated with lower large- and small-airway function.[20] Our findings may have significant public health implications in informing environmental and health care policymakers to make greater efforts in clean air actions, so as to reduce the burden of asthma associated with ambient particulate air pollution in high altitude areas.

We also identified several risk factors associated with asthma in the high-altitude population. Recent studies have suggested a relationship between asthma and age. Those studies indicated that the prevalence of asthma increased with age,[35-37] consistent with our study. In addition to genetic determinants, the influence of environmental factors also increases with age. Furthermore, it is necessary to pay more attention to older asthma patients who were associated with increased morbidity and mortality. Second, exposure to household mold or dampness in the current residence was found to be an important risk factors for asthma, consistent with a previous report.[38,39] And our study showed that household mold or dampness exposure may aggravate PM exposure associated risks of asthma. Thus, improvement of home environment and ventilation measures should be a crucial strategy for residents in high altitude.

Our study findings also have vital public health implications. First, the sample size of this survey was large and the samples were obtained using a multistage stratified sampling procedure with strict quality control measures throughout the whole process in high altitude areas. And this is the first epidemiological study on asthma in residents aged 15 years or older in high altitude areas of China. It provides data for better prevention and treatment of asthma in the future. Furthermore, another major finding of this study is the risk factors affect to a different degree the prevalence of asthma at high altitude. PM exposures may be the prevented factors for asthma patients, provided more useful information for policymakers to consider more stringent air pollution control measures. Our results demand an increased focus on asthma management for residents living in high altitude to controlling air pollution by ideological attention, policy formulation, and behavioral containment. Several limitations to our study also should be noted. First, as a cross-sectional study, it could not ascertain the causal relationship between PM exposure and asthma. The longitudinal studies are needed in order to determine the relationship. Second, the study may lead to the misclassification of chronic obstructive pulmonary disease as asthma because both diseases present with wheezing, and our results are prone to reporting bias. Third, other environmental factors such as temperature, wind conditions, and barometric pressure may aggravate the PM concentrations. Unfortunately, these data were not collected in our study. Data analysis may not be possible due to limited data.[40,41] Finally, our air pollution of data particulate matter only included $PM_{2.5}$ and PM_{10}, so we could not estimate the effects of other size-specific particulate matters, such as PM_1 on asthma.

Conclusions

In conclusion, our data indicate the prevalence of asthma among a large sample of high-altitude residents aged more than 15 years living at high altitude (3.7%). In addition, we also studied whether PM exposures could be critical risk factors for asthma, particularly those exposed to household mold or dampness. It is feasible to raise awareness of the severity of air pollution and take practical measures to improve the environmental situation.

Abbreviations

PM, particulate matter; $PM_{2.5}$, particulate matter with a diameter $\leq$2.5 μm; PM_{10}, particulate matter with a diameter $\leq$10 μm; CI, confidence interval; SAD, small airway dysfunction; OR, odds ratio; LMICs, low- and middle-income countries; DALYs, disability-adjusted life-years; ATS/ERS, American Thoracic Society and European Respiratory Society; ECRHS, European Community Respiratory Health Survey; MAIAC AOD, Multi-Angle Implementation of Atmospheric Correction aerosol optical depth; MERRA-2, the Modern-Era Retrospective analysis for Research and Applications, Version 2; root-mean-square error (RMSE); CMAQ, Community Multiscale Air Quality; MMEF, maximal mid-expiratory flow; FEF, forced expiratory flow; ANOVA, analysis of variance; IQR, interquartile range; BMI, body mass index; BD, bronchodilator; FVC, forced vital capacity;

FEV_1, forced expiratory volume in one second; SHOW, Survey of the Health of Wisconsin.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions
YG and TS conceived and designed the study. YG and TS supervised the study. ZX and HL did the statistical analysis. SS, XM and RC provide the information about fine particulate matter. ZX drafted the manuscript. ZW, SW, and WM provide advice in the study and are listed in the acknowledgments. All authors contributed to acquisition, analysis, or interpretation of data, revised the report, and approved the final version before submission.

Ethics
The study protocol was approved by the Institutional Review Board and ethics committee of Beijing Hospital (2013BJYYEC-042C-01). Each participant received detailed information about the study and study methods and provided written informed consent for their participation.

Authors' consent for publication
Submission of the article implies that the work described has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, without the written consent of the copyright-holder.

Declaration of competing interest
The authors declare that they have no competing interests.

Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2023.100774.

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