Original article

Environmental risk factor assessment: a multilevel analysis of childhood asthma in China

Fei Li, Ying-Chun Zhou, Shi-Lu Tong, Sheng-Hui Li, Fan Jiang, Xing-Ming Jin, Chong-Huai Yan, Ying Tian, Shi-Ning Deng, Xiao-Ming Shen

Shanghai, China

Background: **Rapid changes in socioeconomic environment and their diverse patterns in China raise a question: how socio-environmental factors affect childhood asthma in China. We performed a multilevel analysis based on a 2005 national survey to understand the association between environmental factors and asthma, and to provide insights on developing prevention strategies.**

Methods: **A multi-center, cross-sectional survey was conducted in 2018 school-aged children chosen from eight Chinese cities. Children of 6-13 years old were chosen randomly from schools of 39 centers in 8 cities. The multilevel analysis was made to assess both individual-level and city-level risk factors. The effect of gross domestic product (GDP) was further investigated by analysis of the factors.**

Results: **Analysis of city-level environmental factors showed that GDP [adjusted odds ratio (OR)=1.88], particulate matter with aerodynamic diameter ≤10 μm (PM_{10}) (adjusted OR=1.37), and average humidity (adjusted OR=1.33) were strong risk factors. Further analysis of the factors decomposed GDP into two major factors, the first represented by urban construction, energy consumption, nitrogen dioxide concentration, and the second represented by health-system coverage. This suggested that the negative effects of GDP outweighed its positive effects on asthma.**

Conclusions: **The prevalence of childhood asthma varies significantly in the eight Chinese cities. Socio-environmental factors such as GDP, PM_{10} and average humidity are strong risk factors controlling individual attributes, suggesting that balance is needed between public health and economic development in China.**

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Key words: **asthma; environmental health; risk factors; socioeconomic factors**

Introduction

Asthma is one of the most common chronic diseases which has caused substantial health care burden worldwide. According to World Health Organization (WHO) estimates, 235 million people suffer from asthma and 255 000 people died of asthma in 2005.[1] In China, several surveys during the last two decades showed a fast increase in asthma prevalence.[2] Although these studies indicated wide geographic variations in asthma prevalence and the variations were likely to be caused by geography-associated environmental risk factors, the association between environmental factors and asthma was not adequately analyzed. Hence, there is a significant relationship between the rapid development of China's economy and fast environmental changes.

To study the risk factors of asthma, we concentrated on individual-level variables such as allergen exposure, access to health care resources, socioeconomic status, and life style. Though these factors may partially explain the disparity in asthma outcomes, their changes are incapable of fully explaining the diverse pattern across different regions in China. In some US-based studies, factors in different geographic and/or social levels were put together and evaluated using multilevel analysis.[3-6] However, no studies have been conducted in China, which incorporated

Author Affiliations: Department of Developmental and Behavioral Pediatrics, Shanghai Institute of Pediatric Translational Medicine, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China (Li F, Jiang F, Jin XM, Deng SN, Shen XM); Shanghai Key Laboratory of Children's Environmental Health, Shanghai Jiaotong University School of Medicine Shanghai, China (Li F, Li SH, Jiang F, Jin XM, Yan CH, Tian Y, Deng SN, Shen XM); The Key Laboratory of Children's Environmental Health, Ministry of Education, China (Li F, Li SH, Jiang F, Jin XM, Yan CH, Tian Y, Deng SN, Shen XM); Department of Statistics and Actuarial Sciences, East China Normal University, China (Zhou YC); School of Public Health and Institute of Health and Biomedical Innovation, Queensland University of Technology, Australia (Tong SL)

Corresponding Author: Xiao-Ming Shen, MD, 1678 Dongfang Road, Shanghai 200129, China (Tel: 86-21-38626161-6020; Fax: 86-21-38626161-6020; Email: xmshen@shsmu.edu.cn)

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factors at multiple levels into one model.

Considering multilevel structures, researchers from the USA and Europe studied neighborhood and/or school level variables, including racial/ethnic make up, socioeconomic status, violence exposure, allergen exposure, in addition to individual-level risk factors and described the asthma variation in those levels.[3-6] However, assessments of environmental factors at the city level were rarely found. Since there were different systems in China's urban and rural areas, and the socio-environmental data were more easily collected in cities, as an initial study, we considered a multilevel model is needed to include both individual attributes and city-level environmental factors to understand the etiology of asthma in China.

Methods

Subjects

This study was a multi-center, cross-sectional study of 6-13 year-old school children chosen randomly from schools of 39 centers in 8 cities: Shanghai, Guangzhou, Xi'an, Wuhan, Harbin, Chengdu, Hohhot and Urumqi. The cities were capital cities of provinces located in four different regions cited in the *2006 China Statistics Yearbook* according to their geographic locations, economic standards, and population densities (Table 1).[7] Why we choose capital cities? In China, capital cities generally have higher levels of health care and public awareness of allergic diseases compared to other cities or rural areas within the same province, thus the reporting of allergic conditions and risk factors would be more reliable. Three to ten districts were randomly selected from each city, and 1-2 elementary school(s) from each district of the city. Since the selection was proportional to size, the number of districts was determined by the sizes of the 8 cities, and the number of schools was determined by the sizes of the districts.

Data collection

The survey was conducted by The Key Laboratory of Children's Environmental Health in Shanghai, China. A national steering committee which comprised highly experienced pediatricians and epidemiologists from each survey center was established; a uniform research protocol was used by each survey center; and formal training for the survey interviewers was provided. Each questionnaire was completed by a parent or guardian of a child after an informed consent form was signed. To ensure credibility and accuracy of the survey, we randomly selected 239 children for re-evaluation of responses one month after the initial evaluation. A total 123 questionnaires for testing parallel consistency (the consistency between the results when father

Table 1. City description

Cities	Characteristics
Shanghai	Shanghai is the largest economic and financial center in China, and also China's largest industrial center, science and technology center, and external and internal transportation hub. With a subtropical maritime monsoon climate, Shanghai has average annual temperature of 17.1 ºC and average annual relative humidity of 70% in 2005. The total area of the city is 6543 km² of which 100% is urban area. By the end of 2005, the city's total population had grown to 13.6026 million.
Guangzhou	Guangzhou, the capital of Guangdong Province, is a regional central city in South China, and China's southern gateway to the world. It has historically been China's leading commercial port, and is adjacent to Hong Kong and Macao. Guangzhou belongs to subtropical monsoon climate with plenty of rainfall and is evergreen in four seasons. The average annual temperature is 22.8ºC and average annual relative humidity of 71% in 2005. The total area of the city is 7343 km² of which 52.3% is urban area. The total population is 7.5053 million in 2005.
Xi'an	Xi'an, the capital of Shaanxi Province, is a world-renowned historical and cultural city in northwest China. Xi'an is also an important base for scientific research, higher education, industry of the national defense in China's central and western regions. Xi'an has a temperate monsoon climate with average annual temperature of 15.0ºC and average annual relative humidity of 60% in 2005. The total area is 10 108 km² of which 35.4% is urban area, The total population is 7.4173 million in 2005.
Wuhan	Wuhan, the capital of Hubei province, is an industrial and economic center in central China. It is also China's transportation hub. Wuhan belongs to subtropical humid monsoon climate. There are abundant rainfall and distinctive four seasons. The average annual temperature is 17.8ºC and average annual relative humidity is 69%. Wuhan occupies a land area of 8494 km² with 100% being urban area. The total population is 8.0136 million in 2005.
Harbin	Harbin, the capital of Heilongjiang province, is the economic, education, science and technology center in northeast China. It has entered into "top 10 China's cities with most comprehensive strength". Harbin belongs to the temperate continental monsoon climate with the average annual temperature of 4.7ºC and average annual relative humidity of 62%. The total area is 53 068 km² with 8.1% being urban area. The total population is 9.7484 million.
Chengdu	Chengdu, the capital of Sichuan province, is a regional economic and cultural center in southwest China. It is recently ranked as one of "top 10 China's cities with most comprehensive strength". Chengdu belongs to a subtropical humid monsoon climate, featured with four distinct seasons, annual temperature of 16.2ºC, and annual relative humidity of 78%. The total area is 12 163 km², of which urban area is 2176 km². The total population is 10.8203 million in 2005.
Hohhot	Hohhot, the capital of the Inner Mongolian Autonomous Region, is a regional city with high growing speed. The city is inhabited by the 36 ethnic groups including the Mongolians as the main body. Hohhot has temperate continental monsoon climate with average annual temperature of 7.7ºC and average annual relative humidity of 46%. Hohhot has a total land area of 17 224 km² with 11.9% being urban area. The total population is 2.1349 million.
Urumqi	Urumqi, the capital of Xinjiang Uygur Autonomous Region, is a transportation hub of China connecting central Asia and Europe. It is also an important gateway in west China. Urumqi belongs to temperate semi-arid continental climate, with average annual temperature of 7.5ºC and average annual relative humidity of 56%. The city has total area of 10 900 km² with 60.9% being urban area. The total population is 1.415 million.

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and mother completed the same survey at the same time) and 116 questionnaires for assessing test-retest reliability were completed. The internal consistency of overall questionnaire was good (Cronbach's alpha's coefficients were 0.73). The parallel consistency between mother and father was represented by intro-class correlation coefficients (ICCs)=0.89, and the test-retest reliability was also high (ICCs=0.85). There were 23 791 children from six grades in the chosen schools who participated in the study, of whom 22 018 (92.55%) returned completed questionnaires. We excluded 1250 participants who had missing data of either dependent variables or independent variables considered.

Outcome variables

We used key questions from the International Study of Asthma and Allergies in Children questionnaire to examine the prevalence of current asthma. Subjects with asthma were identified as reported by one of the child's parents or guardians. The question regarding asthma was: "Has the child had asthma in the past 12 months?" (Yes or no).[8]

Individual-level variables

All individual-level variables were those have been found to be associated with asthma in prior studies.[9] They belonged to demographic information, health conditions, socioeconomic status, life style, etc., including specific variables such as age, gender, city, diagnosed gastroesophageal reflux (GER), diagnosed obesity, diagnosed recurrent otitis media, snoring, mode of delivery, exclusive breast feeding, intake of carbonated drinks, diagnosed childhood attention deficit hyperactivity disorder (ADHD), diagnosed allergic rhinitis, diagnosed eczema, diagnosed prepartum and postpartum depression, family structure, household income per capita, parental education level, common cold, sleep-disordered breathing, frequent computer use for amusement, and schoolwork burden. The variables related to health conditions were dichotomous based on answers "yes" or "no" to the specific questions. Other variables were as follows: mode of delivery was categorized as vaginal or caesarean, exclusive breast feeding was categorized as "≥4 months" and "<4 months", intake of carbonated drinks was categorized as "≥5 times a week" and "<5 times a week", family structure was categorized as "nuclear family" or "single-parent or extended family", household income per capita was categorized as "≥1500 RMB/year" and "<1500 RMB/year", parental education level was "≥high school graduate" and "<high school graduate", common cold was ">5 times/year" and "<5 times/year", frequent computer use for amusement was "≥5 times/week" and "<5 times/week", and schoolwork burden was "heavy" and "not heavy".

Additional variables

In addition to field-collected data, environment-related variables, which were obtained at the city level, were retrieved later from official database.[7,10] These variables were categorized as natural environmental factors and socioeconomic factors. The natural environmental factors included altitude, humidity variation, temperature variation, average temperature, and average humidity. The socioeconomic factors included gross domestic product (GDP), nitrogen dioxide (NO_2), sulphur dioxide (SO_2), particulate matter <10μm (PM_{10}), urban construction, standard coal consumption, and health-system coverage. Table 2 shows definitions of these factors. In particular, according to a recent study, health-system coverage was identified as a composite measure of coverage constructed with simple averages of 11 interventions

Table 2. Definition of city-level variables in the multilevel model

Variables	Definition	Category
Altitude (m)	The average height of city above sea level on earth	Nature
Average temperature (ºC)	The average annual temperature	Nature
Average humidity (%)	The average annual relative humidity (relative humidity is defined as the percentage of the water vapor density to the saturation water vapor density)	Nature
Temperature variation (ºC)	The difference between maximum and minimum monthly temperature	Nature
Humidity variation (%)	The difference between maximum and minimum monthly relative humidity	Nature
PM_{10} (mg/m³)	The concentration of particles matter less than 10 microns in diameter in the air	Socioeconomics
SO_2 (mg/m³)	The concentration of sulphur dioxide in the air	Socioeconomics
NO_2 (mg/m³)	The concentration of nitrogen dioxide in the air	Socioeconomics
GDP (million RMB)	The monetary value of all of a nation/region's goods and services produced within a nation region's borders and within a particular period of time, such as one year, usually excluding payments on foreign investments	Socioeconomics
Health-system coverage (%)	A composite measure to summarize the overall pattern of health intervention delivery at national and provincial levels	Socioeconomics
Urban construction (%)	Percentage of the land used for urban development and construction	Socioeconomics
Standard coal consumption (million ton)	Amount of energy consumed by a country or city, usually represented by the standard coal equivalent	Socioeconomics

Unit of measurement is indicated in brackets next to variable name. GDP: gross domestic product; NO_2: nitrogen dioxide; SO_2: sulphur dioxide; PM_{10}: particulate matter <10μm.

to summarize the overall service delivery at regional level, which included access to safe drinking water, access to sanitary toilets, smoking cessation, antenatal care, hospital delivery, postnatal care, immunization, examination of suspected tuberculosis cases, treatment of confirmed tuberculosis cases, treatment of hypertension, and effective treatment of hypertension.[10]

Statistical analysis

The outcome of asthma was coded as a binary variable (present/absent). Binary logistic regressions with single individual-level independent variable were used and variables were selected (P<0.05). With these selected individual-level variables X_i, our first model was a fixed effect logistic model where "city" was treated as a fixed effect:

$$\log it\,(\pi_i) = \log\left(\frac{\pi_i}{1-\pi_i}\right) = \beta_0 + \beta_1 X_i + \beta_2\,\mathrm{cit}\,y_i + e_i$$

where π_i is the probability of having asthma for subject i and e_i is the random differential of subject i. Stepwise procedure was used to select risk factors at the individual level and to assess their influence on asthma by calculating odds ratios (ORs). The probabilities for variable entry and removal were 0.05 and 0.10, respectively.

In order to investigate city-level risk factors, our second model was a two-level mixed effect model, where "city" was treated as a random effect, to disclose both the effects of city-level variables and the variation among cities:

$$\log it\,(\pi_{ij}) = \log\left(\frac{\pi_{ij}}{1-\pi_{ij}}\right) = \beta_0 + \beta_1 X_{ij} + \beta_2 X_j + u_j + e_{ij}$$

where π_{ij} is the probability of having asthma for subject i located at city j, X_{ij} represents individual-level variables and X_j represents city-level variables. The parameter u_j represents the random differential at the city level and e_{ij} represents the random differential at the individual level. These differentials were each assumed to have an independent and identical distribution across cities and individuals with variances σ_u^2 and σ_e^2, respectively.

For city-level variables that were correlated, hierarchical cluster analysis was applied to cluster them into less-correlated groups (correlation <0.4). Representative variables were selected from each group and included the multilevel model. Factor analysis was also used to disclose major factors underlying key variables that had impacts on asthma outcome.

We used SAS 9.2 to implement the analysis. The multi-level analysis was performed using PROC MIXED in SAS.

Results

In binary logistic regression analysis of single independent variables, 19 variables were selected (P<0.05) as factors influencing asthma. When a stepwise fixed effect logistic model was used, 17 of the 19 variables were selected (Table 3). Among them, "city" was the most significant factor, followed by maternal education level, gender, ADHD, etc. With Urumqi as the reference category for "city", the prevalence rate of asthma in Shanghai was the highest (adjusted OR=4.48), followed by Chengdu (adjusted OR=3.16), Wuhan (adjusted OR=2.82) and Guangzhou (adjusted OR=2.06) (P<0.05). Harbin, Xi'an and Hohhot were not statistically different from Urumqi in the prevalence rate of asthma (P>0.05) (Table 3).

To identify the effects associated with "city", particularly environment-related effects, 12 city-level environmental variables were chosen according to

Table 3. Values of city-level variables in the eight Chinese cities

Variables	Harbin (4)	Shanghai (10)	Guangzhou (4)	Xi'an (3)	Wuhan (4)	Chengdu (5)	Hohhot (5)	Urumqi (4)
City-level asthma prevalence (%) (95% CI)	1.4 (1.0-1.9)	7.2 (6.4-8.0)	3.0 (2.4-3.6)	1.1 (0.6-1.6)	3.6 (2.8-4.4)	4.5 (3.8-5.3)	1.0 (0.6-1.5)	1.5 (1.0-2.1)
City-level variables								
Altitude (m)	171.7	4.5	6.6	396.9	23.3	505.9	1063	917.9
Average temperature (ºC)	4.7	17.1	22.8	15.0	17.8	16.2	7.7	7.5
Average humidity (%)	62	70	71	60	69	78	46	56
Temperature variation (ºC)	39.5	25.9	16.2	28.1	26.8	20.8	36.2	40.2
Humidity variation (%)	31	15	33	29	22	14	35	45
PM_{10} (mg/m³)	0.10	0.09	0.09	0.13	0.12	0.13	0.10	0.11
SO_2 (mg/m³)	0.04	0.06	0.05	0.04	0.05	0.08	0.05	0.12
NO_2 (mg/m³)	0.06	0.06	0.07	0.03	0.05	0.05	0.04	0.06
GDP (million RMB)	18 304 514	91 541 800	51 542 283	12 701 400	22 380 000	23 707 644	7 436 618	5 625 007
Health-system coverage (%)	48.78	61.35	51.73	47.64	49.33	51.52	44.83	34.43
Urban construction (%)	318	2401	735	231	225	333	144	176
Standard coal consumption (million ton)	32 032 900	80 556 784	40 202 981	14 098 554	30 884 400	24 181 797	14 129 574	15 300 019

*: data presented in city name and the districts select randomly from it. GDP: gross domestic product; NO_2: nitrogen dioxide; SO_2: sulphur dioxide; PM_{10}: particulate matter <10 µm; CI: confidence interval.

their relevance and data availability. To study the inter-correlations among these city-level variables, data for 29 Chinese cities were collected and hierarchical clustering was applied to cluster these variables into five groups with average Pearson's product-moment correlation coefficients between groups <0.4. The largest group had five variables: GDP, energy consumption (represented by standard coal), urban construction, NO_2 concentration and health-system coverage; all were socio-economic variables (Fig).

Representative variables were selected from each group: altitude, average humidity, GDP, SO_2, and PM_{10}. To compare these variables which were of different scales, we used *z*-scores in the two-level mixed effect model. Among the five city-level variables, GDP was the most significant (OR=1.89), followed by PM_{10} (OR=1.37) and mean humidity (OR=1.33) (Table 4).

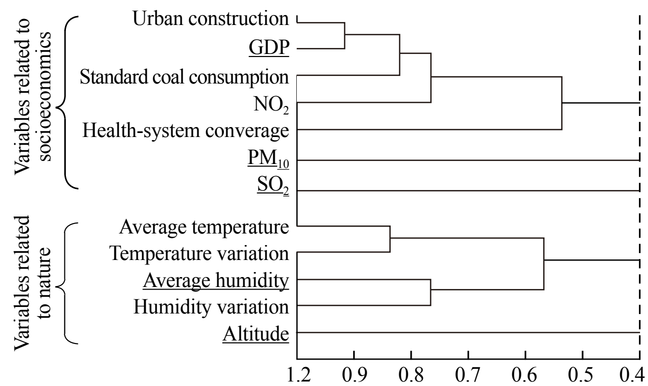

Fig. Hierarchical clustering of 12 city-level environmental variables. Twelve variables including five natural environmental variables and eight socioeconomic variables were clustered into five groups with between group correlations less than 0.4. Underlined variables [gross domestic product (GDP), sulphur dioxide (SO_2), particulate matter <10 µm (PM_{10}), average humidity and altitude] were representative variables of each group that were included in the multilevel model.

Table 4. Assessment of risk factors using fixed effect model and multilevel model

Category	Subcategory	Fixed effect model OR (95% CI)	Multilevel model OR (95% CI)
Fixed effects			
Intercept		**0.00 (0.00-0.00)**	**0.00 (0.00-0.00)**
Individual-level variables			
Gender	Male	**1.56 (1.32-1.85)**	**1.55 (1.30-1.83)**
Diagnosed gastroesophageal reflux	Yes	**2.26 (1.23-4.16)**	**2.30 (1.26-4.22)**
Diagnosed obesity	Yes	**1.67 (1.07-2.58)**	**1.65 (1.06-2.56)**
Mode of delivery	Caesarean (Ref.)		
	Vaginal	**0.87 (0.73-0.99)**	**0.86 (0.72-0.98)**
Carbonated drinks intake	≥5 times/wk	**2.01 (1.43-2.81)**	**1.96 (1.40-2.75)**
Diagnosed childhood ADHD	Yes	**1.50 (1.09 -2.06)**	**1.50 (1.09-2.06)**
Family structure	Single-parent and extended family (Ref.)		
	Nuclear family	**0.84 (0.71-0.99)**	**0.84 (0.71-0.99)**
Household income per capita	≥1500 RMB/mon	**1.57 (1.23-2.02)**	**1.55 (1.21-1.98)**
Maternal education level	≥High school graduate	**1.96 (1.44-2.69)**	**1.95 (1.43-2.68)**
Maternal education level and household income per capita	≥High school graduate and ≥1500 RMB/mon	**1.53(1.05-2.23)**	**1.51 (1.04-2.20)**
Common cold	>5 times/y	**3.11 (2.63-3.69)**	**3.09 (2.61-3.65)**
Sleep-disordered breathing	Yes	**2.13 (1.56-2.90)**	**2.16 (1.59-2.95)**
Paternal snoring	Yes	**1.22 (1.09-1.45)**	**1.22 (1.03-1.45)**
Paternal age at child's birth		**1.03 (1.02-1.05)**	**1.03 (1.01-1.05)**
Diagnosed allergic rhinitis	Yes	**4.59 (3.84-5.48)**	**4.51 (3.78-5.39)**
Diagnosed eczema	Yes	**2.96 (2.36-3.72)**	**2.93 (2.33-3.68)**
City	Urumqi (Ref.)		
	Shanghai	**4.48 (2.99-6.70)**	
	Guangzhou	1.47 (0.95-2.30)	
	Xi'an	1.31 (0.95-2.30)	
	Wuhan	**2.82 (1.78-4.47)**	
	Chengdu	**3.16 (2.08-4.83)**	
	Harbin	1.29 (0.79-2.11)	
	Hohhot	0.96 (0.53-1.71)	
City-level variables (*z*-scores)			
Gross domestic product			**1.89 (1.63-2.19)**
Particulate matter <10µm			**1.37 (1.18-1.60)**
Mean humidity			**1.33 (1.17-1.51)**
Sulphur dioxide			0.95 (0.83-1.09)
Altitude			1.13 (0.93-1.38)
Random effects			
Sigma_u			0.18 (0.11-0.25)
Sigma_e		0.01 (0.01-0.01)	0.01 (0.01-0.01)
Goodness of fit			
Log likelihood		-2316.3	-2300.6

ADHD: attention deficit hyperactivity disorder; OR: odds ratio; CI: confidence interval.

Table 5. Factor analysis of city-level variables which were clustered into the same group as gross domestic product

Factors	Factor I	Factor II
NO_2	**0.77**	0.21
Urban construction	**0.87**	-0.39
Standard coal consumption	**0.91**	-0.25
Health-system coverage	0.77	**0.52**

The table shows the coefficients of the two major factors extracted. Factor I: standard coal consumption, urban construction, and nitrogen dioxide (NO_2) concentration; Factor II: health system coverage.

To further investigate the composite effects of GDP, we made factor analysis of the variables that were closely correlated with GDP. Two major factors were extracted (eigenvalues >0.5) (Table 5). Factor I represented by standard coal consumption, urban construction, and NO_2 concentration, which were considered as risk factors of asthma; Factor II represented by health-system coverage, which was considered as a protective factor of asthma. Thus, the negative effect of GDP outweighed its positive effect on asthma.

Discussion

The cross-sectional survey reveals a geographic variation in the prevalence of asthma in different regions of China, with the highest prevalence rate of 7.2% in Shanghai and the lowest rate of 1.0% in Hohhot. In this survey, we also examined the associated factors of childhood asthma in China at both individual and city levels.

The individual-level factors can be categorized into biological conditions (mode of delivery, sleep disordered breathing, paternal age at child birth), life-style (diagnosed obesity, carbonated drinks intake), socioeconomic status (maternal education level, household income per capita, family structure), and health conditions (common cold, diagnosed ADHD, diagnosed allergic rhinitis, diagnosed eczema, diagnosed GER, paternal snoring). These findings added to the evidence that factors in these categories contribute to explaining the variation of asthma prevalence in China.

Using the fixed effect model with "city" as an independent variable, we found that "city" was the most significant factor contributing largely to the variation of asthma outcome. This prompted us to explore the sub-factors under "city". Thus, we selected 12 city-level environmental variables, including five natural environmental variables and seven socioeconomic ones. We found that there was a large variation in these variables among the 8 cities (Table 3). We intended to understand how the variation in these variables affects the prevalence of asthma.

Our findings were consistent with the reported data showing that socioeconomic factors, such as GDP, are associated with the prevalence of asthma.[11] In contrast to the report that there was a relatively weak positive association between asthma and socioeconomic factors,[11,12] we found a strong influence of GDP on asthma prevalence; furthermore, the composite effect of GDP may be decomposed into positive and negative effects on asthma. Apparently, the negative effect of GDP outweighed its positive effect, thus GDP was shown to be a risk factor for asthma. Indeed, the increase of GDP leads to the improvement of health-system coverage,[10,13] which enhances asthma control; however, the increase of GDP is also positively correlated with worsening envirmental pollution in China, which makes asthma is harder to control. China's GDP has been increasing rapidly during the past 20 years. Thus, the analysis of GDP-related risk factors is important for policy-making regarding public health and city development, while maintaining a reasonable increase of GDP.[14]

As a major source of air pollution in China,[15] PM_{10} was also shown to be a significant risk factor in the present study. PM_{10} is the particulate component of air pollution that can enter the lungs, deposit in the airways and also penetrate into the periphery of the lungs. Several pathways have been proposed to contribute to the asthmatic response and could be amplified by PM_{10} exposure. These include the ability to cause inflammation with subsequent tissue damage, neurogenic stimulation with increased smooth muscle constriction and airway inflammation, and direct stimulation of lipid mediators and mucus, which contribute to airway narrowing and blockage respectively. China's PM_{10} has far exceeded the international standard (Global Air Quality Guide) that was formulated by the WHO.[16,17] High PM_{10} concentrations were considered to be related to the coal-centerd energy structure and large-scale urban construction.[15]

The significant effect of outdoor average humidity represented influence from the climate, since average humidity was closely related to average temperature, temperature variation and humidity variation in our study. Thus, the asthma outcomes were affected by both natural environment and socioeconomic environment. The mechanisms, directly or indirectly, by which outdoor average humidity may affect the manifestation of asthma in children were not clear. Considering outdoor average humidity is a strong determinant of indoor relative humidity, we thought it was likely that outdoor average humidity may affect the prevalence of asthma symptoms through the indoor relative humidity, which was associated with some high risk factors of asthma prevalence, such as indoor exposure to dust mites, home dampness and moulds.[12]

There are several limitations of the present study

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which may bias the results. Firstly, all the sampling sites were cities, thus only representing urban areas. Further research is expected to be performed outside urban areas. Secondly, since most of information was obtained from the questionnaire, some biases such as memory recall bias were unavoidable. Thirdly, because this study was initially designed to address the issue of childhood sleep, there were some important allergic risk factors that were not included, for example, family history of asthma and allergies, and indoor and outdoor environmental factors such as indoor temperature, indoor humidity, household dust, pollen exposure, etc. Fourthly, it was also difficult to determine the major site of indoor activities of school-age children among residence, school and other places.

In conclusion, our findings revealed that the prevalence of childhood asthma varied geographically in China. By controlling individual attributes, we found that socio-environmental factors such as GDP, PM_{10} and average humidity were strongly associated with the prevalence rate of asthma, suggesting that a careful balance is needed between public health and economic development in China.

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Ethical approval: This study was approved by the local institutional review boards of Shanghai Jiaotong University School of Medicine, Sichuan University West China Center of Medical Sciences, Sun Yat Sen University Medical School, Huazhong University of Science and Technology Tongji Medical University, Xi'an Jiaotong University College of Medicine, Harbin Medical University, Inner Mongolia Medical College and Xinjiang Medical University. We obtained written informed consent forms from all the parents/guardians of the children involving in the study.

Competing interest: None declared.

Contributors: This study was planned and implemented by Shen XM, who was the principal investigator. He was responsible for overall conception and design of the study as well as acquisition of funding. Li F contributed to the conception and design of the study, analysis and interpretation of data, critical revisions of the manuscript for important intellectual content, and clinical diagnostic expertise for the study. Li SH, Jiang F, Jin XM, Yan CH, Tian Y and Deng SN implemented the study and made critical revisions of the manuscript for important intellectual content. Li F and Zhou YC contributed equally to this work.

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