Global Journal of Health Science; Vol. 9, No. 6; 2017
ISSN 1916-9736 E-ISSN 1916-9744
Published by Canadian Center of Science and Education

Associations between Parental Health, Early Life Factors and Asthma, Rhinitis and Eczema among Pre-School Children in Chongqing, China

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Received: August 29, 2016 Accepted: October 21, 2016 Online Published: November 22, 2016

doi:10.5539/gjhs.v9n6p121 URL: http://dx.doi.org/10.5539/gjhs.v9n6p121

Abstract

Purpose: To study associations between parental factors and children's asthma, rhinitis and eczema.

Methods: Parents of 3-6 years old children in Chongqing, China answered a questionnaire on parental history of asthma/allergies, parental symptoms and children's asthma, rhinitis and eczema. Associations were analyzed by multiple logistic regression.

Results: Among 4250 children (response rate: 74.5%), 8.4% had doctor-diagnosed asthma (DD asthma); 6.2% doctor-diagnosed allergic rhinitis (DD rhinitis); 20.4% wheeze; 19.4% cough; 37.9% rhinitis and 13.6% eczema. Among reporting parents (females 70.4%, males 29.6%), 16.2% were smokers; 47.4% reported rhinitis; 54.2% cough; 47.8% skin symptoms; 70.5% fatigue and 48.7% headache.

Parental asthma/allergy was associated with children's DD asthma (OR=3.64) and DD rhinitis (OR=4.23). The associations were stronger for paternal asthma/allergy. Rural children had less DD rhinitis and current rhinitis. Children of mothers who were salespersons during pregnancy had more rhinitis (OR=1.49), children of teachers had more DD rhinitis (OR=2.09) and cough (OR=1.66), children of office workers had more DD rhinitis (OR=2.04) and children of mothers working in hospitals had more DD asthma (OR=2.47). Parental current symptoms were associated with wheeze, cough, rhinitis and eczema among the children with ORs ranging from 1.37 to 2.28 (all $p<0.001$).

Conclusions: Parental asthma/allergy can be a risk factor for asthma or allergy, especially paternal asthma/allergy. Growing up in rural areas can be beneficial for rhinitis. Mother's occupation during pregnancy may influence children's asthma and rhinitis. In questionnaires studies on children's asthma or allergies, the reporting parent's gender and current medical symptoms may influence the results.

Keywords: Pre-school children, asthma, rhinitis, eczema, home environment, rural childhood, occupation, validation, fatigue, headache

1. Introduction

Children's asthma and allergies has increased globally (Chen, 2003; Asher et al., 2006). The international Study of Asthma and Allergies in Childhood (ISAAC) has compared asthma and allergy between different countries (The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee, 1998), and analyzed associations with the home environment (Brunekreef et al., 2012). A recent review suggested that the rise in the prevalence of allergic disorders globally is associated with the whole civilizational progress, which is a complex interplay between immune response, invading pathogens, diversity of environmental factors and genetic background (Rutkowski et al., 2014).

Parental factors can influence the prevalence of asthma, rhinitis and eczema in their children in different ways.

Some studies indicate that father's and mother's occupational exposure may influence childhood asthma and allergies. The fathers' occupational exposure to particle from welding and smoking habits before conception can influence the prevalence of childhood asthma in the offspring (Svanes et al., 2016). Another study found that paternal occupational exposure to flour dust increased the risk of childhood asthma (Tagiyeva et al., 2010). A recent review concluded that the mothers' occupational exposure to airborne chemicals during pregnancy can influence asthma, allergy and eczema in the offspring (McFadden et al., 2013). One Danish study found that if the mother had worked as baker, dental assistant, electric/electronic assembler, sewer/embroider or bookbinder during pregnancy, the offspring had more atopic diseases. Moreover, there was an increased risk of asthma among the children if the mothers had shift work during pregnancy (Magnusson et al., 2006). Another study from Denmark found that maternal occupational exposure to low molecular weight compounds (LMW) known to cause occupational asthma (asthmogens) during pregnancy was associated with a borderline significantly increase of asthma in 7-year-old children (Christensen et al., 2013). One study from United Kingdom found that maternal occupational exposure to latex and/or biocides increase the risk of childhood asthma (Tagiyeva et al., 2010). One study from Taiwan found that children of mothers who worked during pregnancy had an increased risk of atopic dermatitis as compared to mothers who did not work, especially if the mother had a professional or technical occupation (Wang et al., 2013). There has also been concern about the effect of maternal stress during pregnancy on atopic diseases in the child. One recent review identified 16 studies on this topic and concluded that there could be an effect of maternal stress but existing studies are of diverse quality (Andersson et al., 2016). Among the 16 studies, only three had investigated effects of occupational stress. Two of these studies found associations between mothers' job strain during pregnancy and atopic disorders in the children (Larsen et al., 2014; Wang et al., 2013).

Urban and rural areas can be different in terms of environmental exposures and several studies have reported a protective effect of growing up in rural areas (Nilsson et al., 1999; Barnes et al., 2001). Many children in rural areas have parents who are farmers and a protective effect of the farming environment has been suggested. A cross-sectional survey in Germany found that farmers' children had a lower prevalence of hay fever than their peers not living in an agricultural environment (Von Ehrenstein et al., 2000). A birth cohort study in Sweden showed a significantly lower risk of asthma and allergic rhino-conjunctivitis among children of farmers compared to children of non-farmers (Klintberg et al., 2001). The European Community Respiratory Health Survey (ECRHS) demonstrated that early-life farm exposure was related to less atopic sensitisation, atopic asthma and atopic rhinitis as adults (Campbell et al., 2016). The ECRHS study also confirmed that early childhood pets or growing up in a farm were associated with less incidence of rhinitis in adolescence (Matheson et al., 2011). However, there are few studies from China on the potentially protective effect of growing up in the countryside.

It is well known that heredity plays an important role for the development of asthma and allergies. Because of this, most epidemiological studies of environmental risk factors for children's asthma or allergic disease adjust for parental history of asthma or allergy (Renzoni et al., 1999; Bornehag et al., 2004). Epidemiological studies on pre-school children's asthma and allergies are often based on questionnaire data reported by the parents. Parents' current health status or gender may cause reporting bias when parents are reporting children's asthma and allergy. However, if there is an association between parents' current health and childrens' asthma, rhinitis and eczema, it could also be due to the socio-economic status of the family, shared indoor and outdoor environment or common dietary habits. We found very few studies on associations between parents' current medical symptoms and pre-school children's asthma and allergic symptoms and diagnoses reported by their parents. Moreover, we found few studies investigating if there is a reporting bias related to the gender of the parent answering the questions on childrens' asthma or allergy or the family history of asthma or allergy.

The first aim was to study associations between urban or rural childhood, mothers' occupation during pregnancy and parental history of asthma or allergy and pre-school children's health (asthma, rhinitis and eczema). This was done in a study where one parent answered a self-administered questionnaire in a population study in Chongqing, China. Moreover, we investigated associations between parents' gender and current medical symptoms (rhinitis, cough, skin symptoms, fatigue and headache) and their reports on children's asthma, rhinitis and eczema and parental asthma or allergy.

2. Materials and Methods

2.1 Study Population

The present study is a part of an epidemiological multi-center study of asthma and allergies among children in China (China, Children, Homes, Health, CCHH) (Zhang et al., 2013). The questionnaires were distributed to the children's parents or guardians by the teachers in 54 randomly selected kindergartens in Chongqing during December 2010 to April 2011 (Wang et al., 2014). One parent per child (reporting parent) aged from 1-8 years old

were invited to participate in the study. Chongqing is a city with 3.2 million population which is situated in the southwest part of China, with hot summers and cold winters. The current data analysis was restricted to 3-6 years old children where the questionnaire was answered by the parents.

2.2 Ethics Statement

The study and the consent procedure were approved by the Medical Research Ethics Committee of School of Public Health, Fudan University. The participants gave informed consent.

2.3 Questionnaire Data

A slightly modified version of a Swedish questionnaire was used (Bornehag et al., 2004). It included questions on children's gender and age, breast feeding (less or more than 6 months), parental (the child's father or mother) history of asthma or allergy and reporting parents' gender, current smoking and current symptoms (rhinitis, cough, skin symptoms, fatigue and headache). There was also one question about the mothers' job during pregnancy, and one on the location of the home.

Questions about children's health were:

(C1) Has your child ever been diagnosed with asthma by a doctor?

(C2) Has your child ever been diagnosed with hay fever or allergic rhinitis by a doctor?

(C3) In the last 12 months, wheezing or whistling in the chest (children's wheeze)?

(C4) In the last 12 months, dry cough at night for more than two weeks, apart from a cough associated with a cold or chest infection (children's cough)?

(C5) In the last 12 months, problem with sneezing, or a runny, or a blocked nose when he/she did not have a cold or the flu (children's rhinitis)?

(C6) Eczema at any time in the last 12 months (children's eczema)?

Questions about parental history of asthma or allergy (the child's father and mother) were:

(P1) Has the child's father ever had asthma?

(P2) Has the child's father ever had nasal or eye allergies?

(P3) Has the child's mother ever had asthma?

(P4) Has the child's mother ever had nasal or eye allergies?

Parental history of asthma or allergy was defined by if there was at least one positive (yes) answer to any of the four questions above (P1-P4).

Questions about reporting parents' current symptoms in the last 3 months were (Sundell, 1994):

(P5) Irritating, stuffy or runny nose (rhinitis)?

(P6) Cough?

(P7) Dry or flushed facial skin, scaling/itching scalp or ears, or hands dry, itching, red skin? (skin symptoms)

(P8) Fatigue?

(P9) Headache?

There were three options for each answer, 0 = never, 1 = sometimes, and 2 = often (every week).

The mothers' occupation during pregnancy included 10 alternatives: unemployed, housewife, student, farmer, blue-collar worker (industrial worker), salesperson, teacher, office worker, housewife, hospital-related job, and other jobs. The occupations were further divided into eight groups which were: not working (combining unemployed, housewives and students), farmers, blue-collar workers, salespersons, teachers, office workers, hospital-related jobs and other jobs. Mothers' occupation was analyzed as categorical variable coded as not occupationally active=0, farmers=1, blue-collar workers=2, salespersons=3,, teachers=4, office workers=5, hospital related work=6 and other jobs (not specified)=7. Those who were not occupationally active (unemployed, housewives or students) during pregnancy were used as the reference category.

Question about the house site was obtained from the same questionnaire. The question was "where is the current house situated?" There were three alternatives, which were urban, suburban and rural.

2.4 Reporting Parents' Current Symptoms Score

Initially, a score ranging from 0-10 was constructed based on five current symptoms among the reporting parents

in the last 3 months: (1) rhinitis, (2) cough, (3) skin symptoms, (4) fatigue, and (5) headache. Each symptom was scored 0, 1 or 2. From the five types of current symptoms, a parents' symptoms score (0-10) was constructed and classified in three groups. Then a categorized parents' symptom score was calculated, selecting cut-off points to get three groups with approximately similar number of parents in each group (tertiles)): lowest score group if reporting parents' current symptoms score = 0 or 1; middle score group if reporting parents' current symptoms score = 2 or 3 and highest score group if reporting parents' current symptoms score >= 4.

2.5 Statistical Analysis

Statistical analyses were conducted with SPSS 17.0. Initially, associations between parental history of asthma or allergy (none vs. any parent) and children's health were analyzed by multiple logistic regressions adjusting for children's gender, children's age, breast feeding, reporting parents' gender, reporting parents' current smoking, mothers' occupation during pregnancy and house site. Then the same adjustment was applied to analyze the associations between parental history of asthma or allergy (none/only father/only mother/both) and children's health. Then a second model was constructed to analyze associations between parental history of asthma or allergy (none/any parent), parental history of asthma or allergy (none/only father/only mother/both) and children's health, by adding an extra variable, reporting parents' current symptom score (0-10), in the models. Then the associations between reporting parents' gender, mothers' occupation during pregnancy, house site and children's health were analyzed in two mutual adjustment models. The first model included children's gender, children's age, breast feeding, reporting parents' current smoking and parental asthma or allergy (none/any parent). The second model included all the independent variables in the first model as well as one extra variable, reporting parents' current symptoms score (0-10).

Associations between reporting parents' current symptoms and children's health were analyzed by multiple logistic regression adjusting for children's gender, children's age, breast feeding, reporting parents' gender, reporting parents' current smoking, mothers' occupation during pregnancy and house site. Then a second type of model was constructed by adding parental history of asthma or allergy (none/any parent) in the models.

The associations were expressed as odds ratios (OR) with a 95% confidence interval (CI). Analyses are considered to be statistically significant if the p-value is less than 0.05.

3. Results

Totally, 5299 of the 7117 questionnaires were answered (74.5%). The study was restricted to questionnaires answered by the father or the mother and children aged 3-6 y. A total of 1049 questionnaires were excluded, 194 questionnaires were excluded because the children were too young (1 or 2 y old) or too old (7 or 8 y old), 155 because there were no data on children's gender, 392 because there were no data on parent's gender; and 308 were excluded because they were not answered by the father or the mother (answered by other guardians). Thus, 4250 children were included: 48.8% were girls and 55.1% had breast feeding more than 6 months. Among reporting parents, 70.4% were females, 16.2% were current smokers and 5.5% had a history of asthma or allergy.

In the bivariate data analysis (crude analysis), doctor-diagnosed asthma and current wheeze were more common among boys. Mothers had more skin symptoms and headache, but cough was more common among fathers (Table 1). Mothers reported a higher prevalence of doctor-diagnosed rhinitis, cough and eczema among their children (Table 2 and Table 3). Parental asthma or allergy was 6.7%. In our study, one of the parents answered the questionnaire. We investigated if the reporting of paternal and maternal asthma or allergy was the same if you reported for your own health or for the spouses' health. There were no significant difference in paternal asthma or allergy, if reported by the father or his wife. However, the prevalence of maternal asthma or allergy was higher if the mother reported (4.5%) compared to reports by her husband (2.2%) ($p<0.001$). Due to this observation we adjusted for reporting parents' gender in all regression models.

Parental asthma or allergy was associated with children's health. If both father and mother had asthma or allergies, the children had the highest prevalence of doctor-diagnosed rhinitis (38.5%), current cough (38.5%), rhinitis (61.5%) and eczema (50.0%). Children with only paternal asthma or allergy had the highest prevalence of doctor-diagnosed asthma (31.6%) and current wheeze (46.5%) (Table 2 and Table 3). The prevalence of categorized parents' symptoms score were 28.0% for the lowest score group, 34.1% for middle score group and 37.9% for the highest score group. Parents in the highest score group reported the highest prevalence of doctor-diagnosed asthma, current wheeze, cough, rhinitis and eczema among their children (Table 2 and Table 3). A total of 54.1% of the mothers were not occupationally active during pregnancy, 42.4% were unemployed, 11.4% were housewife and 0.3% were students. Children of mothers with hospital-related work had the highest prevalence of doctor-diagnosed asthma and children of mothers with office work had the highest prevalence of

doctor-diagnosed allergic rhinitis (Table 2). Children of mothers who were farmers had the highest prevalence of wheeze, children of teachers had the highest prevalence of cough, children of salespersons had the highest prevalence of current rhinitis and children of office workers had the highest prevalence of current eczema. (Table 3). Children living in rural areas had the lowest prevalence of doctor-diagnosed asthma, doctor-diagnosed rhinitis (Table 2) and current rhinitis (Table 3).

Table 1. Prevalence of doctor-diagnosed asthma and rhinitis and current symptoms among the children and reporting parents' current symptoms (n=4250)

Category	Subcategory		Total n(%)	Male n(%)	Female n(%)	p [a]
Children's health	Doctor-diagnosed asthma		348(8.4)	217(10.2)	131(6.5)	<0.001
	Doctor-diagnosed hay fever or allergic rhinitis		253(6.2)	145(6.9)	108(5.4)	0.052
	Wheeze in the last 12 months		844(20.4)	464(21.9)	380(18.8)	0.013
	Cough in the last 12 months		805(19.4)	409(19.3)	396(19.6)	0.795
	Rhinitis in the last 12 months		1569(37.9)	835(39.2)	734(36.4)	0.066
	Eczema in the last 12 months		562(13.6)	295(14.0)	267(13.3)	0.518
Reporting parents' current symptoms	Rhinitis in the last 3 months	Any	1783(47.4)	509(46.8)	1274(48.0)	
		Weekly	108(2.9)	81(3.1)	27(2.5)	0.506
	Cough in the last 3 months	Any	2045(54.2)	630(56.8)	1415(53.1)	
		Weekly	62(1.6)	36(1.4)	26(2.3)	0.039
	Skin symptoms in the last 3 months	Any	1747(47.8)	462(43.1)	1285(49.8)	
		Weekly	188(5.1)	134(5.2)	54(5.0)	<0.001
	Fatigue in the last 3 months	Any	2767(70.5)	804(69.3)	1963(71.0)	
		Weekly	356(9.1)	243(8.8)	113(9.7)	0.299
	Headache in the last 3 months	Any	1849(48.7)	440(40.3)	1409(52.1)	
		Weekly	79(2.1)	58(2.1)	21(1.9)	<0.001

[a] p by Chi-square test (2×3 Chi-square test for reporting parents' current symptoms).

Table 2. Data on parents' history of asthma or allergies, reporting parents' current symptoms, mothers' occupation and house site, stratified for children's doctor-diagnosed asthma and rhinitis (n=4250)

Category	Subcategory	Total (%)	DD asthma [a] (%)	p [b]	DD rhinitis [c] (%)	p [b]
Reporting parents' gender	Female	70.4	8.9		6.9	
	Male	29.6	7.2	0.069	4.3	0.001
Parents' history of asthma or allergies	None	93.3	6.9		5.0	
	Only father	2.9	31.6		17.3	
	Only mother	3.5	21.9		19.9	
	Both	0.3	23.1	<0.001	38.5	<0.001
Categorized parents' symptoms score [d]	Lowest	28.0	4.9		5.1	
	Middle	34.1	8.4		5.8	
	Highest	37.9	10.3	<0.001	7.4	0.074

Mother's occupation during pregnancy	Unemployed [e]	54.1	7.0		4.6	
	Farmers	5.0	5.2		1.1	
	Salespersons	5.4	8.6		6.0	
	Blue-collar workers	4.6	9.1		5.3	
	Teachers	4.3	9.4		9.5	
	Office workers	15.1	11.6		11.0	
	Hospital-related workers	3.0	19.4		5.7	
	Other	8.4	8.6	<0.001	8.5	<0.001
House site	Urban	71.3	9.3		7.0	
	Suburban	18.8	7.6		5.9	
	Rural	10.0	4.8	0.007	1.5	<0.001

[a] Children with a history of doctor-diagnosed asthma.

[b] *p* by Chi-square test (2×4 Chi-square test for parental asthma or allergy, 2×3 Chi-square test for categorized parents' symptoms score and house site, and 2×6 Chi-square test for mother's occupation during pregnancy).

[c] Children with a history of doctor-diagnosed hay fever or allergic rhinitis.

[d] The categorized parents' symptom score was calculated by selecting cut-off points to get three groups with approximately similar number of parents (tertiles)): lowest score group if reporting parents' current symptoms score = 0 or 1; middle score group if reporting parents' current symptoms score = 2 or 3 and highest score group if reporting parents' current symptoms score >= 4.

[e] Unemployed include those have no job, were housewives or students.

Table 3. Data on parents' history of asthma or allergies, reporting parents' current symptoms, mothers' occupation and house site, stratified for children's current wheeze, cough, rhinitis and eczema (*n*=4250)

Category	Subcategory	Wheeze[a] (%)	*p*[b]	Cough [a] (%)	*p*[b]	Rhinitis [a] (%)	*p*[b]	Eczema [a] (%)	*p*[b]
Reporting parents' gender	Female	20.8		20.3		38.1		14.4	
	Male	19.4	0.330	17.3	0.030	37.4	0.711	11.8	0.026
Parents' history of asthma or allergies	None	18.8		18.6		36.4		13.1	
	Only father	46.5		37.2		55.8		17.7	
	Only mother	30.1		19.0		56.6		14.6	
	Both	30.8	<0.001	38.5	<0.001	61.5	<0.001	50.0	0.001
Categorized parents' symptoms score[c]	Lowest	11.9		11.2		26.2		7.5	
	Middle	17.3		17.0		34.8		11.5	
	Highest	28.1	<0.001	26.7	<0.001	46.9	<0.001	17.6	<0.001

		Unemployed [d]	20.5		18.5		35.5		13.4	
		Unemployed [d]	20.5		18.5		35.5		13.4	
		Farmers	21.9		14.4		36.8		9.5	
		Salespersons	17.0		18.1		46.4		14.2	
Mother's occupation during pregnancy		Blue-collar workers	18.5		22.6		40.8		13.8	
		Teachers	18.3		28.9		44.7		13.0	
		Office workers	20.8		21.1		40.5		14.5	
		Hospital-related workers	19.4		21.0		44.3		11.4	
		Other	23.0	0.746	18.9	0.014	36.2	0.004	17.1	0.392
		Urban	20.5		20.0		39.9		13.7	
House site		Suburban	19.0		18.4		34.6		13.6	
		Rural	22.8	0.326	15.4	0.077	30.5	<0.001	14.1	0.972

[a] Children with wheeze/cough/rhinitis/eczema in the last 12 months.

[b] *p* by Chi-square test (2×4 Chi-square test for parental asthma or allergy, 2×3 Chi-square test for categorized parents' symptoms score and house site, and 2×6 Chi-square test for mother's occupation during pregnancy).

[c] The categorized parents' symptom score was calculated by selecting cut-off points to get three groups with approximately similar number of parents (tertiles)): lowest score group if reporting parents' current symptoms score = 0 or 1; middle score group if reporting parents' current symptoms score = 2 or 3 and highest score group if reporting parents' current symptoms score >= 4.

[d] Unemployed include those have no job, were housewives or students.

As a next step, logistic regression models were applied. Associations between parental asthma or allergy, fathers'/mothers' asthma or allergy and children's health were analysed by using two different models, one with and one without adjustment for parents' current symptoms score. Results were similar in the two models (Table 4). Parental asthma or allergy was associated with doctor-diagnosed asthma and doctor-diagnosed rhinitis among the children. The associations between paternal asthma or allergy and doctor-diagnosed asthma among the children were stronger as compared to the associations for maternal asthma or allergy. Moreover, paternal asthma or allergy was associated with current wheeze, cough and rhinitis among the children (Table 4).

Table 4. Associations between parental asthma or allergy and children's health

Parents' health	Subcategory	DD asthma[a]	DD rhinitis[a]	Wheeze[b]	Cough[b]	Rhinitis[b]	Eczema[b]
		OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)
Parental asthma or allergy[c]	None	1.00	1.00	1.00	1.00	1.00	1.00
	Only father	5.55(3.58,8.61)***	3.39(2.23,6.45)**	3.85(2.60,5.68)**	2.65(1.77,3.95)**	2.28(1.55,3.37)***	1.44(0.88,2.37)
	Only mother	3.31(2.14,5.13)***	3.76(2.36,6.00)***	1.90(1.30,2.79)**	0.95(0.61,1.49)	2.17(1.53,3.09)***	1.11(0.68,1.82)
	Both	3.86(1.26,14.6)*	12.5(3.89,40.1)***	1.69(0.51,5.52)	2.19(0.71,6.77)	2.69(0.87,8.27)	5.87(1.87,18.5)**
Parental asthma or allergy[c]	None	1.00	1.00	1.00	1.00	1.00	1.00
	Any parent	4.06(2.96,5.56)***	4.03(2.84,5.72)***	2.59(1.98,3.38)***	1.61(1.21,2.14)**	2.20(1.70,2.84)***	1.38(0.99,1.92)

Parental asthma or allergy[d]	None	1.00	1.00	1.00	1.00	1.00	1.00
	Only father	5.19(3.18,8.45)***	4.37(2.49,7.67)**	3.01(1.94,4.69)***	2.14(1.36,3.37)**	2.08(1.34,3.22)**	1.21(0.69,2.10)
	Only mother	2.81(1.71,4.60)**	3.52(2.09,5.93)***	1.21(0.78,1.90)	0.68(0.41,1.12)	1.82(1.22,2.70)**	0.70(0.39,1.27)
	Both	4.52(1.10,18.6)*	18.0(4.88,66.6)***	1.09(0.27,4.36)	2.49(0.69,8.98)	3.06(0.77,12.1)	4.66(1.30,16.7)*
Parental asthma or allergy[d]	None	1.00	1.00	1.00	1.00	1.00	1.00
	Any parent	3.64(2.55,5.19)***	4.23(2.87,6.22)***	1.83(1.35,2.49)***	1.25(0.90,1.73)	1.93(1.44,2.57)***	1.02(0.69,1.49)

*** $p<0.001$, ** $p<0.01$, * $p<0.05$.

[a] Children with ever doctor-diagnosed asthma/doctor-diagnosed hay fever or allergic rhinitis.

[b] Children with wheeze/cough/rhinitis/eczema in the last 12 months.

[c] Adjusted for children's gender, age, breast feeding, reporting parents' gender, reporting parents' current smoking, mothers' occupation during pregnancy and house site (urban/suburban/rural).

[d] Adjusted for children's gender, age, breast feeding, reporting parents' gender, reporting parents' current smoking, reporting parents' current symptoms score (0-10), mothers' occupation during pregnancy and house site (urban/suburban/rural).

Moreover, associations between reporting parents' gender, mother's occupation during pregnancy and location of the current home and children's health were analyzed by using two different models, one with and one without adjustment for parents' current symptoms score. Results were similar in the two models, so we only present data from the model including adjustment for parents' current symptom score in the table. Fathers reported less doctor-diagnosed rhinitis among their children. Children of mothers who were salespersons during pregnancy had more current rhinitis, children of teachers had more doctors-diagnosed rhinitis and cough, children of office workers had more doctors-diagnosed rhinitis, children of mothers with hospital-related work had more doctors-diagnosed asthma and mothers with other occupations (not specified) had more doctor-diagnosed rhinitis. Children living in rural areas had less doctor-diagnosed rhinitis and current rhinitis (Table 5). In order to see the possible influence of farm exposure on current rhinitis, we calculated the proportion of mothers working as farmers during pregnancy among those living in rural areas. A total of 18.5% of the mothers living in rural areas had worked as farmers.

Table 5. Associations between reporting parents' gender, mothers' occupation during pregnancy and house site and children's health in mutual adjust model.

Mutual adjustment model [a]	Subcategory	DD asthma[b]	DD rhinitis[b]	Wheeze[c]	Cough[c]	Rhinitis[c]	Eczema[c]
		OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)
Reporting parents'gender	Female	1.00	1.00	1.00	1.00	1.00	1.00
	Male	0.72(0.48,1.08)	0.54(0.33,0.88)*	0.83(0.63,1.08)	0.89(0.68,1.16)	1.07(0.86,1.31)	1.02(0.76,1.38)
Mother's occupation during pregnancy	Unemployed	1.00	1.00	1.00	1.00	1.00	1.00
	Farmers	1.03(0.43,2.47)	0.24(0.03,1.78)	1.09(0.66,1.80)	0.66(0.35,1.25)	1.17(0.77,1.79)	0.50(0.23,1.12)
	Salespersons	1.18(0.64,2.18)	1.16(0.56,2.40)	0.68(0.43,1.07)	0.90(0.58,1.39)	1.49(1.07,2.07)*	1.09(0.68,1.77)
	Blue-collar workers	1.36(0.73,2.54)	1.26(0.58,2.73)	0.94(0.61,1.46)	1.20(0.78,1.84)	1.28(0.89,1.82)	0.88(0.52,1.49)
	Teachers	1.26(0.71,2.22)	2.09(1.18,3.70)*	0.81(0.53,1.24)	1.66(1.14,2.42)**	1.37(0.98,1.92)	0.96(0.59,1.56)
	Office workers	1.38(0.97,1.97)	2.04(1.39,2.99)**	0.88(0.68,1.15)	1.04(0.80,1.35)	1.06(0.85,1.31)	0.89(0.65,1.23)
	Hospital-related workers	2.47(1.41,4.32)**	1.15(0.50,2.63)	0.75(0.44,1.28)	0.98(0.59,1.64)	1.23(0.81,1.88)	0.68(0.35,1.32)
	Other	0.91(0.53,1.55)	1.89(1.15,3.12)*	0.91(0.64,1.28)	0.96(0.67,1.35)	1.04(0.79,1.38)	1.17(0.80,1.71)

House site	Urban	1.00	1.00	1.00	1.00	1.00	1.00
	Suburban	0.97(0.67,1.39)	1.06(0.71,1.59)	0.97(0.76,1.24)	0.99(0.77,1.28)	0.84(0.69,1.03)	1.07(0.80,1.42)
	Rural	0.71(0.40,1.27)	0.30(0.11,0.83)*	1.20(0.88,1.65)	0.85(0.60,1.21)	0.69(0.52,0.91)**	1.17(0.80,1.72)

*** $p<0.001$, ** $p<0.01$, * $p<0.05$.

[a] Mutual adjustment model with children's gender, children's age, breast feeding, reporting parents' current smoking, parental asthma or allergy (none vs. any parent), reporting parents' current symptoms score (0-10), reporting parents' gender, mother's occupation during pregnancy and house site in the same model.

[b] Children with ever doctor-diagnosed asthma/doctor-diagnosed hay fever or allergic rhinitis.

[c] Children with wheeze/cough/rhinitis/eczema in the last 12 months.

Finally we analyzed associations between reporting parents' current symptoms and children's health by using two different models, one with and one without adjustment for parental asthma or allergy. Associations between parents' current symptoms and children's current wheeze, cough, rhinitis and eczema remained significant when adjusting for parental asthma or allergy, while the associations between reporting parents' current symptoms and children's doctor-diagnosed asthma or doctor-diagnosed rhinitis were no longer significant (Table 6).

Table 6. Associations between reporting parents' current symptoms and children's health

Current symptoms	Model	DD asthma[a]	DD rhinitis[a]	Wheeze[b]	Cough[b]	Rhinitis[b]	Eczema[b]
		OR(95%CI).	OR(95%CI).	OR(95%CI).	OR(95%CI).	OR(95%CI).	OR(95%CI).
Rhinitis	Model I[c]	1.32(1.04,1.69)*	1.44(1.09,1.90)*	1.91(1.62,2.26)***	1.85(1.55,2.19)***	1.95(1.70,2.24)***	1.64(1.35,2.00)***
	Model II[d]	1.17(0.90,1.51)	1.26(0.94,1.69)	1.85(1.55,2.20)***	1.82(1.52,2.18)***	1.88(1.63,2.17)***	1.60(1.30,1.96)***
Cough	Model I[c]	1.38(1.08,1.76)*	1.41(1.06,1.87)*	1.68(1.42,1.99)***	1.83(1.53,2.18)***	1.74(1.51,2.00)***	1.60(1.31,1.96)***
	Model II[d]	1.23(0.95,1.61)	1.28(0.96,1.72)	1.62(1.36,1.93)***	1.78(1.49,2.14)***	1.68(1.45,1.94)***	1.57(1.28,1.93)***
Skin symptoms	Model I[c]	1.39(1.09,1.78)**	1.37(1.04,1.82)*	2.04(1.72,2.43)***	1.63(1.37,1.94)***	1.52(1.32,1.75)***	2.24(1.82,2.75)***
	Model II[d]	1.26(0.97,1.63)	1.25(0.93,1.67)	2.00(1.67,2.39)***	1.66(1.39,1.98)***	1.45(1.26,1.68)***	2.28(1.84,2.81)***
Fatigue	Model I[c]	1.88(1.39,2.55)***	1.13(0.83,1.55)	1.88(1.54,2.29)***	1.83(1.49,2.25)***	1.63(1.40,1.90)***	2.14(1.67,2.74)***
	Model II[d]	1.71(1.24,2.34)**	0.98(0.71,1.36)	1.80(1.47,2.21)***	1.75(1.42,2.16)***	1.55(1.32,1.81)***	2.16(1.68,2.79)***
Headache	Model I[c]	1.34(1.05,1.71)*	1.18(0.89,1.55)	1.61(1.37,1.91)***	1.81(1.52,2.15)***	1.43(1.25,1.64)***	1.68(1.37,2.05)***
	Model II[d]	1.17(0.90,1.51)	1.00(0.75,1.34)	1.59(1.34,1.89)***	1.77(1.48,2.11)***	1.36(1.18,1.57)***	1.73(1.41,2.12)***

*** $p<0.001$, ** $p<0.01$, * $p<0.05$.

[a] Children with ever doctor-diagnosed asthma/doctor-diagnosed hay fever or allergic rhinitis.

[b] Children with wheeze/cough/rhinitis/eczema in the last 12 months.

[c] Adjusted for children's gender, children's age, breast feeding, reporting parents' gender, reporting parents' current smoking, mothers' occupation during pregnancy and house site (urban/suburban/rural).

[d] Adjusted for children's gender, children's age, breast feeding, reporting parents' gender, reporting parents' current smoking, parental asthma or allergy (none vs. any parent), mothers' occupation during pregnancy and house site (urban/suburban/rural).

4. Discussions

Consistent associations were found between parental asthma or allergy and doctor-diagnosed asthma and rhinitis among the children. Paternal asthma or allergy seems to be more strongly associated with children's asthma or allergies than maternal asthma or allergy. Children of mothers who were salespersons during pregnancy had more current rhinitis, children of teachers had more doctors-diagnosed rhinitis and cough, children of office workers had more doctors-diagnosed rhinitis, children of mothers with hospital-related work had more doctors-diagnosed asthma and mothers with other occupations (not specified) had more doctor-diagnosed rhinitis. Children living in

rural areas had less doctor-diagnosed rhinitis and current rhinitis.

Parental asthma or allergy was associated with children's doctor-diagnosed asthma and doctor-diagnosed rhinitis in this study. A possible explanation to this finding could be shared genetic factors. It is well known that if the parents have asthma or allergy, then the child has a greater risk for developing asthma and allergies (Howard et al., 2000; Zhao et al., 2008). Although heredity plays a major role in asthma and in other allergic diseases, mechanisms underlying the inheritance of these disorders are poorly understood, as is the relative contribution of maternal and paternal conditions to risk of disease among the offspring. Our study found that paternal asthma or allergy seems to be more strongly associated with children's asthma or allergies as compared to maternal asthma or allergy. There is inconsistency in the literature on this issue. One cross-sectional study from Germany found that paternal asthma had a stronger association with children's asthma, while maternal allergic rhinitis had a stronger association with children's allergic rhinitis (Dold et al., 1992). One birth cohort study concluded that maternal allergy increase the risk of allergy in girls while paternal allergy increase the risk of allergy in boys (Arshad et al., 2012). In contrast, one study from Norway showed that the association between maternal asthma/hay fever and childhood asthma was stronger than the association for paternal asthma/hay fever (Jaakkola et al., 2001). Another study from USA found similar results. Maternal asthma was more strongly associated with childhood asthma than paternal asthma (Litonjua et al., 1998). A recent review article concluded that maternal asthma was a greater risk factor for offspring's asthma than paternal asthma (Lim et al., 2010).

Our study indicate that maternal exposure during pregnancy could play a role in the development of asthma and allergies in the offspring. We found that if the mothers' had worked as salesperson, teacher, office workers or in hospitals, their children had more asthma or rhinitis. One limitation of our study is that we have no data on SES of the family, or fathers' occupation. A recent review concluded that social disadvantage in high-income countries was related to a two-fold risk of childhood asthma (Spencer et al., 2015) and poorer asthma control (Kopel et al., 2014). Another systematic review and meta-analysis suggested that childhood asthma is associated with lower SES, whereas the prevalence of allergies is associated with higher SES (Uphoff et al., 2015). Most of the occupations associated with an increased risk of asthma or allergies in our study were white collar workers without any obvious occupational exposure to chemicals. However, hospital-related work can included exposure to chemicals and allergens, including latex, antibiotics and biocides. One previous study found an association between maternal exposure during pregnancy to latex and biocides childhood asthma (Tagiyeva et al., 2010). In addition, many hospital workers have shift work, and a previous study found that mothers shift work during pregnancy was a risk factor for asthma in the offspring (Magnusson et al. 2006). The other maternal occupations associated with an increased risk of childhood asthma or rhinitis in our study (salesperson, teacher, office worker) did not have any obvious exposure to chemicals or allergens. One possible explanation to our findings could be work stress in these occupations, but we did not measure work stress. Further more detailed studies are needed on the role of work stress during pregnancy as a cause of childhood asthma and allergies.

We found that living in rural areas was associated with less rhinitis among the children. Urban and rural areas can be different in terms of environmental exposures, such as air pollution, as well as allergens from pets, animals in farms, pollens, cockroaches and house dust mites. Although many of these exposures can cause allergic sensatisation, a number of studies have reported a protective effect of rural living for children after adjusting for those exposures (e.g. Nilsson et al., 1999; Barnes et al., 2001). One Swedish-Polish study showed that there was an increased prevalence of respiratory symptoms and sensitization to allergens among 10-12 year-old school-children living in urban areas, and suggested that the differences could be explained by air pollution (Braback et al., 1994). We found only two studies from China on this issue. A recent Chinese study in school children found a similar result as in our study namely that self-reported rhinitis was less common among those living in rural areas (Yang et al., 2015). Another Chinese study in school children found that pollen/cat allergy was less common among pupils with a rural childhood (Norback et al., 2007). Since many children in rural areas are exposed to agriculture, a protective effect of the farming environment has been discussed. A number of studies have demonstrated that growing up on a farm can be protective for childhood asthma and allergies (Naleway, 2004, Von Ehrenstein et al., 2000, Klintberg et al., 2001). There can also be a persistent protective effect of growing up on a farm (Campbell et al., 2015). In our study, we have no information on postnatal exposure to the farm environment, just information on the area of the current home, so we cannot specifically evaluate the effect of the farm environment. The rural areas in our study were near the city and only 18.5% of the mothers in these areas had worked as farmer during pregnancy. Moreover, we did not find any significant effect of this farm exposure on rhinitis, suggesting that the beneficial effect of growing up in rural arears was mainly due to other factors such as reduced exposure to air pollution.

Epidemiological questionnaire studies can be affected by selection bias and reporting bias. In this study, we

included all children aged 3-6 years old and the questionnaire was answered by one parent. The children were recruited from randomly selected day care centers in one city. The sample size was reasonably large, and the response rate good (74.5%). However, the cross-sectional study design limits the possibility to draw conclusions on causality. Another limitation is the lack of clinical data and lack of data on the fathers' occupation, which made it impossible to study effects of the socioeconomic status of the family.

Our study is one of few epidemiological questionnaire studies evaluating the role of reporting parents' gender and reporting parents' current health on their reporting of children's asthma and allergies. Fathers reported less doctor-diagnosed rhinitis among their children. Moreover, fathers' reported less asthma or allergy among their wives as compared the wives own reports about their asthma and allergy. This could mean that fathers had less information on their wives and children's medical diagnoses.

Moreover, were also found that the reporting parents' current symptoms were positively associated with reports on children's current wheeze, cough, rhinitis and eczema. There are different possible explanations to the observed association between the reporting parents' health and the childrens' health, including reporting bias, genetic factors, shared home environment, shared outdoor environment, socioeconomic status (SES) of the family or lifestyle factors. The fact that the associations with parental current symptoms were similar for mucosal symptoms (eye, nose, throat) and general symptoms (headache, fatigue) may indicate a general effect due to reporting bias. However, the associations between childrens' health and parental factors (parental asthma or allergy or mothers occupational exposure during pregnancy) did not change when adjusting for parents' current symptoms.

Previous validation studies on children asthma, rhinitis and eczema have compared parental reports och childrens' asthma or allergies with doctor-diagnosis (gold standard). Two studies found high specificity (Strina et al., 2010; Hedros et al., 2007) one found high positive predictive value (Braun-Fahlander et al., 1997), one found high sensitivity (Vissing et al., 2012) and one found both high specificity and high sensitivity (von Kobyletzki et al., 2012). Since there is usually some deviation between parental reports and doctors-diagnosis of asthma, rhinitis or eczema, there is a possibility of reporting bias. Further studies are needed measuring parental health by clinical methods or by doctors diagnose to evaluate the role of reporting bias in relation to questionnaire data on pre-school childrens' asthma and allergies.

Shared indoor or outdoor environment could be another reason for the observed associations between parental medical symptoms and childrens' asthma, rhinitis and eczema. Further studies are needed to test the "shared environment hypothesis" assessing indoor and outdoor environmental data by objective inspection and exposure measurements.

5. Conclusions

Growing up in rural areas can be protective for rhinitis. Parental asthma or allergy were associated with doctor-diagnosed asthma and rhinitis among children. Paternal asthma or allergies can have a stronger influence on asthma or allergies in their offspring. Mothers' occupation during pregnancy can be an important early life factor associated with children's asthma and rhinitis. In questionnaires studies on children's asthma or allergies, the reporting parent's gender and current medical symptoms may influence the results. Adjustment of parents' gender and current symptoms should be considered besides the common adjustment for parental asthma or allergy. Further studies with clinical diagnosis, genetic information, objective measurements of home environment/outdoor environment and information on the socioeconomic status of the family are needed.

Acknowledgments

The study has been supported by the National Technology Support Project (2012BAJ02B06), the 111 Project (No.B13041), and "the Short-term International Academic fund" of Chongqing University 2015 Overseas Visiting Student Project (No.GJXSFX150210). The authors would like to give thanks to the support of the CCHH workgroup in Chongqing. Thank you to all the parents who filled out questionnaires, and teachers from kindergartens who provided assistance for our survey.

Competing Interests Statement

The authors declare that there is no conflict of interests regarding the publication of this paper.

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