



Home environment and diseases in early life are associated with allergic rhinitis

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ABSTRACT

Objective: Risk factors in relation to allergic rhinitis (AR) remain unclear despite considerable interest. This study aimed to analysis the relationship between home environment and diseases in early life and AR.

Methods: In a case-control survey, 242 AR patients and 258 healthy persons responded to questionnaires designed to capture pre-pregnancy/pregnancy diseases, maternal medication usage, diseases in early life of participants, family allergic history and home environmental factors. Forty risk factors potentially connected with AR were investigated and analyzed with chi-square test and logistic regression.

Results: There was no correlation between mother's disorders such as periodontitis, chronic rhinitis, diabetes etc. and AR ($p > 0.05$). A logistic regression analysis showed that neonatal jaundice ($p < 0.001$), respiratory system infection ($p < 0.001$), diarrhea ($p < 0.01$), eczema ($p < 0.01$) in the early life and home environmental factors such as house decoration ($p < 0.01$), mold environment ($p < 0.001$), keeping flowers and plants ($p < 0.001$), passive smoking ($p < 0.01$) were associated with AR.

Conclusion: Diseases in early life and home environment are closely associated with AR.

1. Introduction

AR is a common atopic disease, the incidence of which has increased with the progress of industrialization, modern lifestyle and increased pollution. AR has become a global health problem affecting 10%–20% of populations [1] (up to 40% of children), most especially in developed countries [2]. At present, there has been substantial research on the pathogenesis of AR, but the exact factors associated with AR remain unclear. Indeed, studies often contradict each other.

AR is thought to be related to a variety of factors, such as obesity [3,4], feeding patterns, mode of delivery [5,6], periodontitis during pregnancy [7], etc. Caesarean section and artificial feeding may be risk factors for childhood asthma and AR [8], although some investigators have found no association between breast feeding and allergic disorders [9]. Hsieh et al. [7] suggested that gum infection in women during pregnancy is an independent risk factor for allergic diseases in children. Recent studies found that medicine use early in life, such as paracetamol, antibiotic may be a risk factor for AR and other allergic diseases [10,11]. Researches shown that rural populations from developing countries performed lower allergy-related disorders prevalence, and exposure to environmental pollution are more important to the etiology of allergy-related disorders [12,13].

Environmental factors, both indoor and outdoor, may play an important role in AR development [14,15]. Factors like parental allergic disease [16], antibiotic use in pregnancy [17], neonatal jaundice [18], and others also may have relationships with AR.

The risk factors of AR are complex and controversial, even there has a lot of literature about it. We had conducted a questionnaire about 40 items, attempted to explore the potential risk factors for AR. Our questionnaire contained the diseases and medication use in pregnancy or pre-pregnancy of the respondents' mothers, diseases of the respondents in the first 6 months of life, family allergy history and home environment, some of which were rarely reported such as the relationship between AR and hypertension, diabetes, abnormal thyroid function in pregnancy or pre-pregnancy. The objective of the present study was to explore the risk factors and epidemiological characteristics of AR and to provide an effective basis for early prevention and intervention.

2. Methods

2.1. Study population

Our study carried out on a group of 762 participants and eventually

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500 completed questionnaires were accepted (242 AR, 258 control). A total of 378 questionnaires were sent to AR patients with response rate of 64.02% and 384 questionnaires were sent to control group with response rate of 67.19%. Experienced otolaryngologists made the diagnosis of AR based on symptoms such as nasal congestion, rhinorrhea, sneezing and itching, alongside physical examination findings of pale and edematous nasal mucosa. Additionally, AR patients had SPT (ALK-Abelló, Hørsholm, Denmark) $\geq$ “+” or serum sIgE $\geq$ 0.7 kU/L (uniCAP Pharmacia, Uppsala, Sweden). The aeroallergens used for both SPT and serum sIgE included *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*, dog fur, cat fur, *Blattella germanica*, *Alternaria tenuis*, *Aspergillus niger*, *Artemisia argyi*, ragweed, *Humulus lupulus*, *Platanus acerifolia*, willow, *Populus tremula*, *Ulmus pumila* and birch. AR patients accompanied with asthma or allergy related disorders were excluded. The control group was recruited from a routine physical examination population without any nasal symptoms, and people with respiratory diseases, allergic disorders, immune related diseases were excluded. All participants were recruited from the Department of Otorhinolaryngology Head and Neck Surgery at the First Affiliated Hospital of Nanchang University (Jiangxi province, China) from Jan. 2017 to Dec. 2017, which is the largest hospital in Jiangxi province. The participants came from all over the province and about 5% of the patients came from neighboring provinces. All AR patients were treated at this hospital, some of them treated with specific immunotherapy, and some just with medication.

2.2. Assessment questionnaires

The 40 items in the questionnaire we used are presented in Table 1. We assessed home remodeling or renovation in early life such as floor installation, new furniture, wall covering, painting, addition of particleboard or suspended ceiling [19]. We asked about signs of mold growth in the home (any surfaces other than food), flowers or other plants kept indoors, presence of animals: both family pets, such as dog, cat, bird, as well as farm animals, such as chicken, duck, or goose. Active smokers (current smokers) had smoked at least one cigarette per day or one cigar a week for the past year [20]. Passive smoking or non-smoking means that the infants within 6 months lived in smoky environment or not. Diseases such as periodontitis, rhinitis, diabetes, abnormal thyroid function, hypertension and so on were identified by outpatient or inpatient medical records. The reliability of our questionnaire was assessed by internal consistency and test-retest. For internal consistency reliability, the Cronbach α value was estimated from questionnaire item responses. Test-retest reliability was assessed by computing the interclass correlation between our questionnaires performed at the baseline and the follow-up visits. Criterion validity of our questionnaire was evaluated by the Kaiser-Meyer-Olkin test.

Table 1

Four categories of potential risk factors for allergic rhinitis.

Maternal conditions pre-pregnancy	Maternal conditions during pregnancy	Respondent's characteristics in the first 6months of early life	Other factors of respondent
Periodontitis	Periodontitis	Feeding patterns	Parents' allergic history
Chronic Rhinitis	Chronic Rhinitis	Gestational age	Grandparents' allergic history
Diabetes	Fever	Delivery method	House renovation
Abnormal thyroid function	Antibiotic use	Neonatal jaundice	Mold contamination
Hypertension	Pregnancy complications	Respiratory system infection	Indoor flowers or plants
	diabetes	Diarrhea	Indoor animals
	abnormal thyroid function	Eczema	Smoking
	hypertension	Kawasaki disease	
	intrahepatic cholestasis	Anemia	
	Medications used for treatment	Candida albicans stomatitis	
	hypoglycemics	Urticaria	
	antihypertensives	Urinary tract infection	
	thyroid-related medicines	Antibiotics use	
	insulin injection	Drug allergy	
		Food allergy	

Table 2

General characteristics of enrolled subjects.

Characteristic	Allergic rhinitis N = 242	Control N = 258	Statistic	p
Gender			X ² = 0.555	> 0.05
Male	130	128		
Female	112	130		
Age (y)	12.8 $\pm$ 5.2	13.7 $\pm$ 5.2	z = -1.994	> 0.05
Body mass index (kg/m ²)	19.9 $\pm$ 3.1	19.9 $\pm$ 2.2	z = -0.191	> 0.05
Birthweight (kg)	3.36 $\pm$ 0.36	3.32 $\pm$ 0.21	z = 1.242	0.214

Analysis by z text analysis.

2.3. Statistical methods

We compared the AR group with the control group to explore the potential risk factors of AR. For categorical variables, absolute frequencies and percentages with a 95% confidence interval (95% CI) were obtained, and chi-square tests were performed. The normal distributions were presented as mean $\pm$ standard deviation (SD). Differences were compared using z-test or continuous calibration chi square test, as appropriate.

A logistic regression model was constructed, the variables which had values $p < 0.1$ in univariate analysis were brought into the subsequent model. These variables including pre-pregnancy diseases (2 items: periodontitis and chronic rhinitis); pregnancy-related conditions (3 items: chronic rhinitis, fever, and antibiotic use); conditions in early life especially in the first 6 months after birth (11 items: gestational age, delivery method, diseases in early life); family allergic history (4 items: parental and grandparental allergy); and environmental factors (6 items: living condition, house renovation etc.). Above all, 26 risk factors relationships to AR were analyzed by logistic regression. Results were considered statistically significant at $p < 0.05$. SPSS v. 22 was used for statistical calculations.

2.4. Ethical approval

The study was reviewed and approved by the Institutional Review Board and Research Ethics Committee of the First Affiliated Hospital of Nanchang University. All participants provided informed consent to participate in the study.

3. Results

3.1. Reliability and validity analysis of the questionnaire

The baseline intraclass correlation coefficient and Cronbach α value exceeded 0.70, the test-retest reliability among these patients at the

Table 3
Variables associated with allergic rhinitis in univariate analysis.

Associated factors		Allergic rhinitis		Control		χ2	p
		Yes	No	Yes	No		
Maternal conditions pre-pregnancy							
Periodontitis		11	231	0	258	11.99	0.001
Chronic Rhinitis		27	215	0	258	26.42	0.001
Pregnancy-related conditions							
Periodontitis		8	234	0	258	6.70	0.10 ^b
Chronic Rhinitis		10	232	0	258	8.87	0.003 ^b
Fever		18	224	1	257	18.12	0.00
Antibiotic use		10	232	1	257	0.14	0.004
Pregnancy complication		4	238	0	258	2.47	0.12 ^b
Medication use for pregnancy complication		0	242	0	258	0	> 0.05
Gestational age							
< 37 weeks		13		2		7.556	0.006 ^c
37–41 weeks		229		256			
Feeding pattern							
Breast feeding		129	0	145	0	4.535	0.104
Artificial feeding		63	0	77	0		
Mixed feeding		50	0	35	0		
Delivery manner							
Vaginal delivery		160		156		40.719	0.045
Caesarean delivery		98		86			
Diseases in early life							
Neonatal jaundice		73	169	11	247	59.94	0.00
Respiratory system infection		47	195	11	247	27.98	0.00
Diarrhea		57	185	10	248	41.67	0.00
Eczema		63	179	7	251	56.40	0.00
Kawasaki disease		1	241	0	258	0.001	0.33 ^d
Anemia		1	241	0	258	0.001	0.33 ^d
Candida albicans stomatitis		4	238	0	258	2.468	0.12 ^b
Urticaria		10	232	1	257	8.14	0.005
Urinary tract infection		0	242	0	258	0	> 0.05
Antibiotic use		60	181	24	234	22.96	0.00
Drug allergy		21	221	1	257	21.55	0.00
Food allergy		42	202	4	254	37.34	0.00
Direct relatives' allergy							
Parents' allergy	Maternal allergy	37		2		68.95	0.00 ^a
		33		10			
		7		1			
Grandparents' allergy	Parents allergy	37	205	0	258	43.85	0.00
Living condition							
House renovation		83	159	25	233	41.13	0.00
Mold contamination		62	179	2	256	69.38	0.00
Indoor flowers or plants		90	152	33	225	40.08	0.00
Keeping animals		41	201	16	242	14.26	0.00
Parental Smoking							
Active smoking		4		0		19.839	0.00 ^a
Passive smoking		114		79		19.56	

The others: Pearson χ^2 .

^a Exact: Monte Carlo method.

^b Pearson χ^2 Continuity Correction.

^c Redit

^d Fisher's exact test.

baseline and follow-up visits was 0.87. The results showed that the Kaiser-Meyer-Olkin value was 0.616 and Bartlett spherical test ($\chi^2 = 967.987$, $p = 0.000$), indicated that the data are suitable for factor analysis. Eight common factors were extracted by principal component method, and their cumulative contribution rate to total variance variation was 60.011%. Our questionnaire had demonstrated good reliability.

3.2. General characteristics

The general characteristics of AR and control groups are presented in Table 2. In total, 500 participants (242 AR patients and 258 control participants) completed the questionnaire both upon enrollment and at follow up. We measured weight without shoes or outer clothing (to nearest 0.01 kg) and height (to nearest 0.01 m). Body mass index (BMI)

Table 4
Variables associated with allergic rhinitis in the logistic regression.

Associated factors	OR	95% CI for OR		p
		Lower	Upper	
Maternal conditions of pre-pregnancy				
Periodontitis	0.00			0.998
Chronic Rhinitis	0.00			0.997
Pregnancy-related conditions				
Chronic rhinitis	0.00			0.998
Fever	20.65	2.90	64.88	0.178
Antibiotics use	11.08	1.41	47.20	0.155
Gestational age	7.27	1.62	22.5	0.13
Delivery manner				
Vaginal delivery	1.11	0.77	1.52	1.00
Caesarean delivery	1.13	0.78	1.63	1.00
Diseases in early life				
Neonatal jaundice	9.70	5.00	18.83	0.00*
Respiratory system infection	5.41	2.73	10.71	0.001***
Diarrhea	7.64	3.80	15.36	0.007**
Eczema	12.62	5.648	28.20	0.008**
Urticaria	11.07	1.41	87.20	0.16
Antibiotics use	3.23	1.98	5.51	0.33
Drug allergy	25.70	3.44	72.21	0.11
Food allergy	13.34	4.70	37.81	0.11
Direct relatives' allergy				
Parents' allergy				
Maternal allergy	16.38	5.01	53.52	0.62
Paternal allergy	3.23	1.68	6.21	0.31
Parental allergy	6.72	0.82	55.03	0.39
Grandparents' allergy		0.00		0.997
Living condition				
House renovation	4.87	2.98	7.95	0.01**
Mold contamination	43.38	10.71	183.60	0.00*
Indoor flowers or plants	4.04	2.58	6.32	0.00*
Keeping animals	3.09	1.68	5.66	0.11
Smoking				
Active smoking		0.00		0.999
Passive smoking	1.63	1.14	2.35	0.003**

*Logistic regression, Significance at $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Abbreviations: OR, odds ratio; CI, confidence interval.

Table 5
Variables associated with allergic rhinitis in the logistic regression with $p < 0.05$.

Associated factors	OR	95% CI for OR		p
		Lower	Upper	
Neonatal jaundice	9.70	5.00	18.83	0.00*
Respiratory system infection	5.41	2.73	10.71	0.001***
Diarrhea	7.64	3.80	15.36	0.007**
Eczema	12.62	5.648	28.20	0.008**
House renovation	4.87	2.98	7.95	0.01**
Mold contamination	43.38	10.71	183.60	0.00*
Indoor flowers or plants	4.04	2.58	6.32	0.00*
Passive smoking	1.63	1.14	2.35	0.003**

*Logistic regression, Significance at $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Abbreviations: OR, odds ratio; CI, confidence interval.

was calculated as weight/height [2] (kg/m^2). There were no differences in terms of age, gender, BMI and birthweight between groups.

The most common aeroallergens of the AR patients in our research

included *Dermatophagoides pteronyssinus* (45.45%), *Dermatophagoides farinae* (36.36%), and *Blomia tropicalis* (31.82%). Some AR patients were allergic to more than 2 aeroallergens.

3.3. Risk factors for AR

Forty potential risk factors of AR were tested in univariate models. We found no statistically significant differences in pre-pregnancy conditions including diabetes, abnormal thyroid function, or hypertension. We also found no statistically significant differences in pregnancy-related conditions such as periodontitis, pregnancy complications (diabetes, abnormal thyroid function, hypertension and intrahepatic cholestasis) or medication use for pregnancy complications (such as hypoglycemics, antihypertensives, thyroid medications and insulin injection). Some conditions in early life (in the first 6 months after birth) showed no statistical differences between the two groups, including feeding patterns, Kawasaki disease, anemia, *Candida albicans* stomatitis and urinary tract infection. The details are shown in Table 3.

However, 24 factors with $p < 0.1$ in the univariate analyses were then incorporated into the logistic regression analysis. We found strong statistical associations between AR and neonatal jaundice, respiratory system infection, diarrhea, and eczema. Environmental factors including house renovation, moldy environment, indoor flowers and plants, and passive smoking were closely related to subsequent AR. The results of the logistic regression analysis are presented in Table 4. Simplified results with only the variables that had $p < 0.05$ were shown in Table 5.

4. Discussion

The present study is first one in this part of China focusing on the relationship of pregestational as well as gestational diseases and AR in children and analyzed the relationship between conditions of early life as well as environmental factors on the subsequent development of AR.

Only a few prior investigations have assessed the correlation between neonatal jaundice and the onset of AR. Wei et al. reported the connections between neonatal jaundice and the development of AR in early childhood [18]. Sun et al. first found the association between neonatal jaundice and AR and asthma [21]. In our study, patients with neonatal jaundice were more likely to develop allergic rhinitis. The mechanism of how neonatal jaundice might affect or even initiate allergic diseases is not clear. It has been suggested that bilirubin may inhibit the Th1 cell response, and intracellular accumulation of unconjugated bilirubin may inhibit the production of IL-2 [22]. A reduction in the level of IL-2 would skew the Th1/Th2 balance toward Th2, thereby increasing the risk of developing allergic diseases. The relationship and mechanism of neonatal jaundice with AR requires more research.

We found a correlation between respiratory tract infections in early life and the development of AR, although the underlying mechanisms are unknown. Previous research supported the epidemiological data that viral respiratory infection may contribute to allergic sensitization [13,14]. Our findings were consistent with those of previous studies [23–25].

In our study, we found that diarrhea in early life had a positive correlation with the later development of AR. The role of intestinal microbiota in the development of atopic disorders has been explored [26]. Immature gut microbiota can be clinically asymptomatic, locally symptomatic (e.g., diarrhea), or systemically symptomatic (disseminated infection) [27]. Microbial exposures could alter the risk of subsequent allergic disease in many cases [28].

Consistent with previous work [29], our study supported that atopic eczema in early life, especially in the first 6 months, is a risk factor of subsequent AR. It has been shown that the main risk factor for childhood AR is not eczema itself, but the allergic sensitization in early life [30] that is central to atopic eczema. However, the causative mechanisms still need more research.

The significant correlation we found between house renovation and AR is in agreement with other studies [31]. Indoor renovation materials and recent home renovation have been associated with an increased incidence of AR and other respiratory symptoms [32,33]. The underlying mechanism between home renovation and AR is unclear; however, some explanations have been proposed. Substantial evidence suggests that many relevant materials, including paints, furniture varnish, and synthetic carpets, can emit chemical substances [34] such as polyvinyl chloride (PVCs).

Our results revealed that keeping flowers or plants indoor, similar to house decoration, was another potential risk factor for AR. Alm et al. suggested pollen was the most commonly reported trigger, followed by indoor animals in school age children [29]. Our results differed. In our research, keeping pets at home was not related to subsequent AR. Our study is the first to explore the relationship between indoor flowers and plants and subsequent AR.

Some epidemiologic evidence has supported that mold exposure may increase the risk of AR in children [35,36]. Our research also supports this. We found that exposed mold was positively correlated with increased incidence of AR. Though the mechanisms for the effects of mold exposure remain unclear, our results fit the hypothesis that moldy odor, resulting from increased levels of microbial volatile organic compounds, may increase the risk of respiratory allergic symptoms [37].

Compared with active smoking and no smoking, we found that passive smoking was closely related to AR ($p = 0.003$). Environmental tobacco smoke impairs children's respiratory health. Burke et al. suggested that exposure to second-hand smoking was associated with an increased risk of asthma and wheeze incidence [38]. Lin Z et al. discovered that exposure to tobacco smoke in the first 2 years of life was positively associated with new onset of symptoms and negatively associated with remission of symptoms [39]. Prescott et al. demonstrated that many of the (over 2000) potential toxic substances in cigarette smoke could cause significantly higher numbers of IgE + Th2 cells and eosinophils in the nasal mucosa in children, which could further trigger inflammation in the lower respiratory tract [40].

Even we try our best to do this research, this study still had several limitations. Recall bias is possibility for all items, such as diseases of the respondents, environmental factors in the first 6 months of life. Even we can clearly define diseases with medical records, there still may be some participants without records who can't remember whether they suffered from diseases or not, it would result in recall bias. In addition, no evaluation of family economic and educational status of respondents would lead to bias. Although all participants were accompanied by professionals to fill out the questionnaires, different family economic and education status would lead to different understanding of the questionnaire, which may still cause misunderstanding bias more or less. At last, different to the cross-sectional survey, all the respondents were recruited from hospital rather than different communities, and the about 65% completion rates of our survey may not represent the real situation of the whole population.

5. Conclusions

Certain diseases in infancy, home renovation, visible mold, indoor flowers/plants, and passive cigarette smoke exposure all increased the risk of subsequent AR in children in southern China. Because this was a case-control study, it could not verify causal influences and incidence rates. Further studies of the mechanisms of these AR risk factors maybe provide new and comprehensive insights into AR prevention and treatment.

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