



Original Article

Comparison of food allergy prevalence among Chinese infants in Chongqing, 2009 versus 1999

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Abstract *Background:* Food allergy prevalence is increasing in developed countries, but these results have not yet been verified in developing countries, especially in China. Our aim was to determine whether the prevalence and characteristics of food allergy have changed over the last 10 years in Chongqing, China.

Methods: Two cross-sectional studies were performed, 10 years apart (1999 and 2009) using the same diagnostic methods in the same age group (0–24 months) of the same clinic in Chongqing, China. A total of 401 infants were randomly selected for the present study. Food allergy was confirmed by food challenge. SPSS 15.0 was used to analyze the difference in prevalence.

Results: Food allergy prevalence increased significantly from 3.5% in 1999 to 7.7% in 2009 ($P = 0.017$). The prevalence of a positive skin-prick-test response was also increased (from 9.9% to 18%; $P = 0.002$). Egg and cow's milk were still the most common food allergens, which cause skin and gastrointestinal symptoms in most infants.

Conclusion: This is the first study in China to indicate time trends in food allergy prevalence and characteristics. Our data show that in the 10-year period from 1999 to 2009, the prevalence of food allergy seems to have increased in China.

Key words comparison, cross-sectional study, food allergy, prevalence.

Allergy is one of the most common chronic diseases that endanger children's health. Epidemiological studies demonstrate that there has been a continuous increase in the prevalence of allergic diseases in Western and Westernized societies over recent decades,^{1,2} including food allergy (FA).^{3,4} However, studies of the prevalence and clinical features of FA from developing countries, including China, are insufficient.⁵ In addition, many studies from developed countries focus on peanut allergy because it is one of the most common food allergens inducing anaphylaxis. In contrast, peanut and tree nut allergies appear to be rare in Asia, possibly due to different eating habits.⁵ Therefore, there is an urgent need for data on the local prevalence and time trends of general food allergy in China.

Between May 1999 and June 1999, we conducted the first study to estimate the prevalence of FA in China. The prevalence of FA was found to be 3.5% among infants.⁶ In that study, egg and cow's milk were the major allergens, and skin symptoms were the most common symptoms; an atopic family history, eczema in early life and early supplementary food introduction were found to be important risk factors in FA prevalence.^{6,7} However, our

study did not evaluate prevalence over time, and it is difficult to compare our results with other studies because of different methodologies, diagnostic criteria, sampling frames and non-response bias. Therefore, there are no reliable data on whether FA prevalence is increasing with rapid Westernization and economic development in China.

To determine whether the prevalence of FA is changing, we conducted a second prevalence study between January and February 2009, using an identical methodology and sampling frame to our 1999 study. In this study, we compared the prevalence and characteristics of infancy FA using data derived from cross-sectional surveys held in 1999 and 2009.

Methods

Sampling frame

In order to investigate time trends in the prevalence of FA, the study was repeated with the same diagnostic methods in the same age group (0–24 months) at the same clinic in 2009. Children aged 0–24 months were enrolled randomly when they received well-baby checking in the division of Primary Child Care, Children's Hospital, Chongqing Medical University. Because FA seems to be age-related, the infants studied in 2009 were similar in age distribution prevalence to those in our original study. A total of 401 infants were involved in this study. There were 218 boys and 183 girls. Of these, 175 were 0–6 months, 142 were 6–12 months, and 84 were 12–24 months. This study was

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Criteria for diagnosis of food allergy

All FA infants were confirmed by food challenge.

At first, a questionnaire was distributed to parents to determine whether the infants had suspected atopic symptoms related to food. The questionnaire inquired about the characteristics and reproducibility of the symptoms, duration between the ingestion and occurrence of the symptoms, and estimated quantity of suspected food. The demographic details, atopic family history and living environment were queried as well.

After that, all subjects underwent a skin-prick test (SPT). The SPT was performed by our nurse in the presence of an allergist, using the prick technique and glycerinated food extract supplied by Greer Company (Taibei, China) according to the standard guidelines.⁸ Food extracts included milk, egg, peanut, soy, fish, shrimp, wheat and orange, which can cause approximately 85% of adverse reactions in children. The positive and the negative control tests with histamine phosphate (10 mg/mL) and saline, respectively, were always placed along with the test allergens. SPT was defined as positive when the greatest diameter of the wheal was at least 3 mm larger than a negative control at 15 min.

Then, a special diet record form was given to those with positive SPT response. Initially, infants continued to have their regular diet for 2 weeks and then suspected foods were eliminated completely from their regular diet for 1–2 weeks. Cow's milk was substituted by extensively hydrolyzed formula (Alfa-re, Nestle, Chongqing, China) in bottle-fed infants who reacted to cow's milk formulas. The parents recorded the contents and amount of all foods eaten by the infant, and symptoms that occurred during this procedure. If the symptoms of the infant did not improve, FA were excluded; however, if the symptoms improved, an open food challenge (OFC) was conducted in the hospital under the supervision of an allergist, as previously described.⁹ In brief, the suspected food was administered with minimal weight first (usually started with about 1/16 of the challenge dose) and then the weight of the food was increased gradually (the interval for increasing the dose was according to the history). For most infants, we increased the dose every 15–30 min, until the usual dietary weight was given. For example, for suspected cow's milk allergy, a drop of the formula was put on the infant's lips first. If no reaction occurred

after 15 min, the formula was given orally and the dose was increased stepwise (0.5, 1.0, 2.0, 5.0, 10, 20, 40, 80, 100, 150 mL) every 15–30 min. The infant was observed for at least 2 h in the clinic before going home. The allergist recorded the respiratory rate, heart rate, blood pressure and any symptoms. Parents were told to observe the child for late reactions at home also. Likewise, boiled eggs, noodles for wheat, cooked soybeans, peanut butter, cooked fish and shrimp, and fresh orange were used for oral provocation. All the suspected foods were investigated one-by-one with the OFC. Once the symptoms were induced by a suspected food, FA was confirmed.

Statistical analysis

As the aim of this study was to compare the prevalence of two cross-sectional studies, we used the same equation to recalculate the prevalence, which is a little different from that of our epidemiology study.⁶ That is, prevalence estimates were calculated by dividing infants with positive results by the total number of completed questionnaires. To compare the differences in SPT positive rate, FA prevalence and other characteristics of FA between the two studies, the *t*-test and χ^2 -test were performed. $P < 0.05$ was considered significant. The SPSS software package version 15 for Windows (SPSS, Chicago, IL, USA) was used for all statistical analysis.

Results

General information of two cross-sectional studies

In the 1999 study, 314 questionnaires were completed and infants underwent the SPT. Ten of the infants dropped out during the food elimination test. Therefore, 304 infants were included in the final analysis with an overall response of 96.8% (304/314). In the present study, 401 questionnaires were distributed and 382 infants were included in the final analysis. The overall response rate was 95.3% (382/401), similar to the 1999 study ($P > 0.05$) (Table 1). The age and sex distribution of infants is shown in Table 1. The age and sex distributions of the study groups were similar in the two studies.

The feeding schedule, age of solid food introduction, and symptoms reported by parents are shown in Table 2. There were no differences in feeding practices between these two decades ($P > 0.05$).

Table 1 Demographic data in the 1999 and 2009 surveys

	1999 study (<i>n</i> = 314)		2009 study (<i>n</i> = 401)		<i>P</i> -value
	<i>n</i>	%	<i>n</i>	%	
Responder					
Full responder	304	96.8%	382	95.3%	0.296
Partial responder	10	3.2%	19	4.7%	
Age					
0–6 months	133	42.4%	175	43.6%	0.878
7–12 months	117	37.2%	142	35.4%	
13–24 months	64	20.4%	84	20.9%	
Sex					
Male	181	57.6%	218	54.4%	0.381
Female	133	42.4%	183	45.6%	

Table 2 Feeding practice and reported symptoms

	1999 study		2009 study		<i>P</i> -value
	<i>n</i>	No. of FA	<i>n</i>	No. of FA	
Feeding methods up to 4 months of age					
Breast-fed	126	7	168	21	0.067
Partially breast-fed	86	3	132	8	0.536
Formula-fed	102	1	101	2	1.000
Age of solid foods introduction					
<4 months	120	5	34	0	0.585
4–6 months	107	5	196	23	0.062
>6 months	31	0	58	6	0.173
Non-introduction	56	1	113	2	1.000
Parents reported symptoms					
Eczema or wheal	27	10	57	29	0.464
Swollen eyelid and lips	1	1	2	1	1.000
Vomiting/diarrhea	15	1	7	2	0.530
Milk refusal	2	1	1	1	1.000
Sneezing or wheezing	2	1	1	0	1.000

FA, food allergy.

There were 31 infants in the 1999 study and 72 infants in 2009 with positive SPT. Some infants were sensitive to a variety of foods (Table 3). However, only four infants in 1999 and three infants in 2009 were diagnosed as having multi-food allergy.

In these two cross-sectional studies, identical methodology was used to obtain the prevalence of FA. The results of diagnostic tests of FA are shown in Table 4. The prevalence was 3.5% in the 1999 study and 7.7% in the 2009 study, respectively.

Prevalence

The parent-reported FA, SPT response and confirmed FA in 1999 and 2009 are compared, respectively, in Table 5. The rate of parent-reported FA increased from 13.7% (1999 study) to 16.7% (2009 study), but there was no statistical significance ($P > 0.05$). Positive SPT response was significantly higher in 2009 (18.0%) than in 1999 (9.9%) ($P < 0.05$). The prevalence of confirmed FA increased markedly from 3.5% (1999 study) to 7.7% (2009 study) ($P < 0.05$). The prevalence of FA in this population increased more than 2.2-fold between 1999 and 2009.

Food allergens and symptoms

The characteristics of FA infants are shown in Tables 5 and 6. The most common triggers of infant FA in Chongqing were egg (9/11 in 1999, 20/31 in 2009) and cow's milk (5/11 in 1999, 14/31 in 2009). The other offending foods included peanut (1/11), soy (1/11), orange (1/11) and fish (1/11) in the 1999 study, while there was no other implicated foods besides egg and cow's milk in 2009.

The prevalence of egg allergy was about 2.9% (9/314) in 1999 and 5.0% (20/401) in 2009, and the prevalence of cow's milk allergy was about 1.6% (5/314) in 1999 and 3.5% (14/401) in 2009. However, the prevalence of infants' FA increased with time and there was no discernible change in the proportion of infants allergic to any one food in these two studies ($P > 0.05$). In 1999, there were four infants with multi-FA out of 11 with FA. In the 2009 study, there were three infants with multi-FA among 31 with FA, which was remarkably lower than that in 1999 ($P < 0.05$) (Table 5).

In both studies the most common symptoms occurred on the skin (10/11, 90.9% of patients in 1999, 27/31, 87.1% in 2009), such as eczema and wheal, followed by gastrointestinal (GI)

Table 3 Distribution of positive skin prick tests (SPT)

	Egg	Milk	Peanut	Fish	Orange	Wheat	Shrimp	Soy
Positive no. of SPT in 1999	23	10	1	1	3	1	0	3
Positive no. of SPT in 2009	62	25	6	3	0	2	1	2

Table 4 The results of diagnostic tests of food allergy

	Questionnaire		SPT		Elimination test		OFC		Prevalence (%)
	Total no.	Positive no..	Total no.	Positive no.	Total no.	Positive no.	Total no.	Positive no.	
1999 study ($n = 314$)	314	43	314	31	31	21	21	11	3.5
2009 study ($n = 401$)	401	67	401	72	72	45	45	31	7.7

OFC, open food challenge; SPT, skin prick tests.

Table 5 Time trend of prevalence of parent-reported FA, positive SPT response and FA

	1999 study (<i>n</i> = 314)		2009 study (<i>n</i> = 401)		<i>P</i> -value
	Positive number (<i>n</i>)	%	Positive number (<i>n</i>)	%	
Reported FA	43	13.7%	67	16.7%	0.268
SPT	31	9.9%	72	18.0%	0.002
FA	11	3.5%	31	7.7%	0.017
Cow's milk allergy	5	1.6%	14	3.5%	0.117
Egg allergy	9	2.9%	20	5.0%	0.154
Multi-FA	4	1.3%	3	0.7%	0.041

FA, food allergy; SPT, skin prick tests.

symptoms (2/11, 18.2% vs 4/31, 12.9%), for example vomiting and diarrhea. Respiratory symptoms were rare in both studies: only one infant showed respiratory symptoms (sneezing) in 1999. All symptoms were confirmed by the OFC.

Discussion

According to some reports, the prevalence of food allergy is increasing along with other allergic diseases.^{10,11} However, there is a lack of data from developing countries, especially China. The primary aim of this study was to determine whether the prevalence and characteristics of food allergy had changed over a 10-year period in Chongqing, China. Therefore, we compared the results of our two cross-sectional studies using the same diagnostic methods on the same age group (0–24 months) in the same clinic in Chongqing.

Most prevalence studies based on self-reported symptoms related to FA range from 9.1% to 34.9%.^{12–14} In our data, although there was no statistical difference ($P > 0.05$), the prevalence of parent-reported FA in 2009 was slightly higher than that in 1999 (16.7% vs 13.7%). During the last few years, FA education programs for the general population and medical personnel in Chongqing have been developed. These educational programs have made people more aware about food allergens and their symptoms. Therefore, this rising trend may be explained by increased knowledge of FA and of the atopic symptoms.¹⁵ Another reason might be because parents in the 2009 study might prefer to consider all adverse reaction to food as FA. In fact, questionnaire-based prevalence studies could overestimate data: it is reported that only 10% of self-reported reactions are confirmed when the food challenge is used.¹⁴ However, it is an important tool to provide information regarding FA.

It is known that FA cannot be diagnosed with SPT alone because the positive predictive value is less than 50%. A positive SPT response merely indicates food sensitization. However, studies have shown that the magnitude of the SPT has a good correlation with challenge-derived hypersensitivity data.^{16–18} Therefore, infants with positive SPT response, especially in those

with atopic family history, are the high-risk population to present clinical symptoms. In these two studies, the food challenge was used to confirm the true FA. With regard to the prevalence of FA, in a recent meta-analysis, the authors observed a marked heterogeneity in the prevalence of FA that could be a result of differences in study design or methodology, or differences between populations.¹⁹ Hereby, it is hard to compare one study to another. To solve this problem, we compared our two studies conducted with the same methodology and almost the same population in the same clinic. We show that the prevalence of positive SPT response and true FA are both increased (from 9.9% to 18% and from 3.5% to 7.7%, respectively), which is consistent with recent reports in developed and developing countries.^{10,11,20} The rapid economic development, environmental changes caused by rapid Westernization and increase in hygiene may partially explain this rising trend in the prevalence of FA.^{21,22} Other hypotheses include topical sensitization, cesarean section, increased use of antacid medication in infants, food processing methods, vitamin D exposure, alterations in dietary fat consumption, and perhaps even delayed introduction of allergenic food.^{4,23}

From our data, the prevalence of egg allergy and cow's milk allergy were not different in these two studies. The most frequently allergenic food sources in infants were egg (9/11 in 1999, 20/31 in 2009) followed by cow's milk (5/11 in 1999, 14/31 in 2009), which is consistent with most countries,²⁴ and somewhat different from Australia, where the top three sensitization food allergens in children under 5 years were shellfish, milk and egg.²⁵ Peanut and shellfish allergy are rare in Chongqing. This profile could be due to our eating habits and food preparation methods compared with those in Australia.

Skin reactions were the most frequent symptoms in infants with FA (10/11, 90.9% of patients in 1999, 27/31, 85% of patients in 2009), followed by GI symptoms. No anaphylactic shock related to FA was found in our study, probably due to the scarce reaction to nuts and shellfish in our population.

In conclusion, the prevalence of FA has increased significantly in 2009 when compared with the previous study in 1999. Egg and

Table 6 Symptoms of food allergy

	1999 study (<i>n</i> = 11)		2009 study (<i>n</i> = 31)		<i>P</i> -value
	Positive	%	Positive	%	
Skin symptoms	10	90.9%	27	87.1%	0.737
Gastrointestinal symptoms	2	18.2%	4	12.9%	0.667

cow's milk are still the first two food allergens for Chinese infants, and the most common symptoms are skin and GI reactions. These data may significantly contribute to our further understanding of FA in childhood in China, and further studies are needed to elucidate the risk factors related to the increase in FA prevalence.

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References

- 1 International Study of Asthma and Allergies in Childhood Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998; **351**: 1225–32.
- 2 Gupta R, Sheikh A, Strachan DP, Anderson HR. Time trends in allergic disorders in the UK. *Thorax* 2007; **62**: 91–6.
- 3 Branum AM, Lukacs SL. Food allergy among U.S. children: Trends in prevalence and hospitalizations. *NCHS Data Brief* 2008; **10**: 1–8.
- 4 Mullins RJ, Dear KB, Tang ML. Characteristics of childhood peanut allergy in the Australian Capital Territory, 1995 to 2007. *J. Allergy Clin. Immunol.* 2009; **123**: 689–93.
- 5 Shek LP, Lee BW. Food allergy in Asia. *Curr. Opin. Allergy Clin. Immunol.* 2006; **6**: 197–201.
- 6 Hu Y, Li HQ. [Prevalence of food hypersensitivity in 0–24 months old infants in Chongqing.] *Chin. J. Pediatr.* 2000; **38**: 431–4 (in Chinese).
- 7 Hu Y, Li HQ, Wang RH. [The influential factor analysis by logistic regression on the result of food skin prick test in children.] *Chin. J. Pediatr.* 2002; **11**(40): 658–61 (in Chinese).
- 8 Eigenmann PA, Sampson HA. Interpreting skin prick tests in the evaluation of food allergy in children. *Pediatr. Allergy Immunol.* 1998; **9**: 186–91.
- 9 Mukuko T, Nishima S, Arita M *et al.* Guidelines for diagnosis and management of pediatric food allergy in Japan. *Allergol Int.* 2007; **56**: 349–61.
- 10 Grundy J, Matthews S, Bateman B, Dean T, Arshad SH. Rising prevalence of allergy to peanut in children: data from 2 sequential cohort. *J. Allergy Clin. Immunol.* 2002; **110**: 784–9.
- 11 Sicherer SH, Munoz-Furlong A, Sampson HA. Prevalence of peanut and tree nut allergy in the United States determined by means of a random digit dial telephone survey: A 5-year follow-up study. *J. Allergy Clin. Immunol.* 2003; **112**: 1203–7.
- 12 Marrugo J, Hernández L, Villalba V. Prevalence of self-reported food allergy in Cartagena (Colombia) population. *Allergol. Immunopathol. (Madr)* 2008; **36**: 320–4.
- 13 Vierk KA, Koehler KM, Fein SB, Street DA. Prevalence of self-reported food allergy in American adults and use of food labels. *J. Allergy Clin. Immunol.* 2007; **119**: 1504–10.
- 14 Zuberbier T, Edenharter G, Worm M *et al.* Prevalence of adverse reactions to food in Germany – a population study. *Allergy* 2004; **59**: 338–45.
- 15 Ones U, Akcay A, Tamay Z, Guler N, Zencir M. Rising trend of asthma prevalence among Turkish schoolchildren (ISSAC phases I and III). *Allergy* 2006; **61**: 1448–53.
- 16 Hill DJ, Hosking CS, Reyes-Benito LV. Reducing the need for food allergen challenges in young children: comparison of *in vitro* with *in vivo* tests. *Clin. Exp. Allergy* 2001; **31**: 1031–5.
- 17 Sampson HA, Ho DG. Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. *J. Allergy Clin. Immunol.* 1997; **100**: 444–51.
- 18 Sporik R, Hill DJ, Hosking CS. Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children. *Clin. Exp. Allergy* 2000; **30**: 1540–6.
- 19 Rona RJ, Keil T, Summers C *et al.* The prevalence of food allergy: A meta-analysis. *J. Allergy Clin. Immunol.* 2007; **120**: 638–46.
- 20 Chandra RK. Food hypersensitivity and allergic disease: a new threat in India. *Indian Pediatr.* 2003; **40**: 99–101.
- 21 Ben-Shoshan M, Kagan RS, Alizadehfar R *et al.* Is the prevalence of peanut allergy increasing? A 5-year follow-up study in children in Montreal. *J. Allergy Clin. Immunol.* 2009; **123**: 783–8.
- 22 Romagnani S. The increased prevalence of allergy and the hygiene hypothesis: missing immune deviation, reduced immune suppression, or both? *Immunology* 2004; **112**: 352–63.
- 23 Lack G. Epidemiologic risks for food allergy. *J. Allergy Clin. Immunol.* 2008; **121**: 1331–6.
- 24 Sampson HA. Food allergy. *J. Allergy Clin. Immunol.* 2003; **111**: S540–7.
- 25 Hill DJ, Hosking CS, Zhie CY, Leung R, Baratwidjaja K, Iikura Y. The frequency of food allergy in Australia and Asia. *Environ. Toxicol. Pharmacol.* 1997; **4**: 101–10.