

## Original Article

# A cross sectional survey on the prevalence of food intolerance and its determinants in an allergic skin disease population in Bengbu, China

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**Abstract:** This study estimates the prevalence of perceived food intolerance and its related factors among people with allergic skin diseases in Bengbu, China. A total of 446 patients with allergic skin diseases who came to the dermatological department in our hospital to check allergens were enrolled in this investigation. Serum IgG level specific for food was measured by enzyme-linked immunosorbent assay (ELISA). The total positive rate of food intolerance was 66.4%, and the leading intolerance items were egg (51.57%), cow's milk (16.14%), soybean (12.33%), crab (8.52%) and shrimp (6.50%). Males showed significantly higher positive rate for cow's milk and wheat than females and various serum specific IgG level in response to cow's milk and wheat were found in the different genders ( $P < 0.05$ ). In different age groups, the positive rate for cow's milk, crab, wheat and egg showed a different pattern and various serum specific IgG levels in response to cow's milk, crab, egg, wheat, shrimp and tomato were found. The prevalence rate of food intolerance in people with allergic skin diseases was relatively high and egg was the major allergen in this population. Cow's milk and wheat may contribute to allergic skin diseases in different genders and age groups.

**Keywords:** Food intolerance, prevalence, allergic skin disease, food specific serum IgG

## Introduction

Food intolerance (or non-allergic food hypersensitivity) is a harmful reaction that occurs in response to food, or drink. The response produces symptoms, which may occur after a delay, to the food itself or to food additives or other food compounds. One or more organs and systems in the body may be affected. Food intolerance is not a true food allergy because that requires immune mechanisms such as those involving Immunoglobulin E (IgE) antibodies, and food intolerance does not [1].

One method of classification of food intolerances is according to their mechanism [1]. These mechanisms include the absence of specific digestive chemicals or enzymes, for example hereditary fructose intolerance, nutrient absorption abnormalities, for example fructose malabsorption and reactions to chemicals in foods that occur naturally, for example salicylate sensitivity. Drugs derived from plant origins, such as aspirin, can also cause these

reactions. In addition non-IgE-mediated immune responses may also cause food intolerance.

In comparison to a food allergy, a food intolerance is more chronic, but less acute. Also food intolerances are less obvious in their presentation, and generally they are more difficult to diagnose than a food allergy [1]. The symptoms resulting from food intolerance can affect the skin, the respiratory tract, and the gastrointestinal tract (GIT) in isolation or together. The resulting skin reactions may be skin rashes, urticaria (hives) [2], angioedema [3], dermatitis [4], and eczema [5]. In the respiratory tract they may be nasal congestion, sinusitis, pharyngeal irritation, asthma and an unproductive cough. The symptoms found in the GIT include irritable bowel syndrome, intermittent diarrhea, abdominal cramps, gas, nausea, constipation, mouth ulcers [6-8], and possibly anaphylaxis [4].

There are different methods of food intolerance diagnosis including hydrogen breath testing

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**Table 1.** Food intolerance positive rate distribution in all patients

	Positive		P*
	n	(%)	
Gender			0.6034
Male	126	28.25%	
Female	170	38.12%	
Age			< 0.001
< 19	125	28.03%	
19~40	93	20.85%	
41~59	64	14.35%	
≥ 60	14	3.14%	

\*Chi-square test.

**Table 2.** Distribution of positive rate of all 14 food intolerance

Food	Positive	
	n	(%)
Egg	230	51.57
Cow's milk	72	16.14
Soybean	55	12.33
Crab	38	8.52
Shrimp	29	6.50
Wheat	22	4.93
Codfish	21	4.71
Rice	17	3.81
Tomato	16	3.59
Mushroom	15	3.36
Chicken	9	2.02
Pork	8	1.79
Beef	2	0.45
Corn	2	0.45

that can identify lactose intolerance and fructose malabsorption, elimination diets monitored by a professional, and enzyme-linked immunosorbent assay (ELISA) with specific food allergens that can identify IgG-mediated immune responses. When using these techniques care must be taken to identify food intolerance, rather than those patients that suffer from food allergy, and autoimmune disease to allow the appropriate management of the disorder [9].

Here, in the present study, to investigate the prevalence of food intolerance in an allergic skin disease population in Bengbu, China. We recruited 446 patients with allergic skin diseases and 14 food specific serum IgG levels were

measured by ELISA. The association of food intolerance with genders and different age groups was analyzed.

### Materials and methods

#### Subjects

A total of 446 patients (median age: 26 years, from 1 to 87 years, 186 males) with allergic skin diseases who came to dermatological department in the First Affiliated Hospital of Bengbu Medical College (Bengbu, China) to check allergens between September, 2013 and September, 2014 were enrolled in this investigation.

#### Ethical considerations

Patients were included in the study upon providing written informed consent. The study protocol was approved by the local ethics committee and conducted in accordance with the ethical standards laid down in the First Affiliated Hospital of Bengbu Medical College.

#### Food specific serum IgG level measurement

The food allergen-specific ELISA kit, Allerquant 14 Food Additives, for in vitro quantitative analysis of IgG antibodies to 14 unique food additive allergens in human serum was purchased from Biomerica, USA, and its performance was in accordance with the manufacture's instruction. According to the IgG concentrations (< 50 U/mL, 50~100 U/mL, 100~200 U/mL and > 200 U/mL), patients were divided into 3 grades including “- (negative), + (mild), ++ (moderate) and +++ (serious)” in which “+~+++” were defined as positive.

#### Statistic

The analyses were performed with fisher's exact test, Wilcoxon signed rank test, Kruskal-Wallis test and Chi-square test with statistical software SPSS version 17 (SPSS Inc., USA). Two-tailed significance tests were used, and P values < 0.05 were regarded as statistically significant.

### Results

Serum samples from all 446 patients (median age: 26 years, from 1 to 87 years, 186 males) with allergic skin diseases enrolled in this study were collected and IgG antibodies of 14 food

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**Table 3.** Distribution of positive rate of animal and vegetable source food intolerance

Grade	Animal source	Positive		Vegetable source	Positive	
		n	(%)		n	(%)
+	Beef	2	0.43	Corn	1	0.22
	Chicken	8	1.74	Mushroom	11	2.39
	Codfish	18	3.9	Rice	15	3.25
	Crab	37	8.03	Soybean	48	10.41
	Egg	101	21.91	Tomato	14	3.04
	Cow's milk	39	8.46	Wheat	20	4.34
	Pork	7	1.52			
	Shrimp	18	3.9			
	++	Beef	0	0	Corn	1
Chicken		1	0.22	Mushroom	4	0.87
Codfish		2	0.43	Rice	3	0.65
Crab		2	0.43	Soybean	6	1.3
Egg		56	12.15	Tomato	0	0
Cow's milk		19	4.12	Wheat	2	0.43
Pork		1	0.22			
Shrimp		1	0.22			
+++		Beef	0	0	Corn	0
	Chicken	0	0	Mushroom	0	0
	Codfish	1	0.22	Rice	0	0
	Crab	1	0.22	Soybean	1	0.22
	Egg	80	17.35	Tomato	2	0.43
	Cow's milk	15	3.25	Wheat	0	0
	Pork	0	0			
	Shrimp	1	0.22			

**Table 4.** Correlation of food intolerance and gender

Food	Male positive		Female positive		P#
	n	(%)	n	(%)	
Beef	1	0.50%	1	0.40%	1
Chicken	3	1.60%	6	2.30%	0.7408
Codfish	7	3.80%	14	5.40%	0.5013
Corn	2	1.10%	0	0.00%	0.1734
Crab	16	8.60%	22	8.50%	1
Egg	97	52.20%	133	51.20%	0.8481
Cow's milk	41	22.00%	31	11.90%	0.0059
Mushroom	6	3.20%	9	3.50%	1
Pork	1	0.50%	7	2.70%	0.1472
Rice	10	5.40%	7	2.70%	0.2087
Shrimp	6	3.20%	13	5.00%	0.4775
Soybean	19	10.20%	36	13.80%	0.3068
Tomato	9	4.80%	7	2.70%	0.3024
Wheat	14	7.50%	8	3.10%	0.0444

#Fisher's exact test.

specific allergens were measured by ELISA. The total positive rate of intolerance to the 14 foods was 66.4% (296/446). There was no difference found in positive rates between genders ( $P > 0.05$ ), while the distribution of food intolerance was different among different age groups (< 19, 19~40, 41~59 and > 60 years) (Table 1). The distribution of positive rates of all 14 food intolerances, and animal and vegetable sources of food intolerances are shown in Tables 2 and 3. The top 5 positive rates of food intolerance were: egg (51.57%), cow's milk (16.14%), soybean (12.33%), crab (8.52%) and shrimp (6.50%) (Table 2). The lowest positive rates were beef and corn both of which were 0.45%. The positive rates of egg intolerance with all "+~++++" grades were highest in animal source and which were 21.91%, 17.35% and 12.15%, respectively, and the highest positive rate of vegetable source food intolerance of soybean (10.41%) with "+" grade (Table 3).

The positive rates of food intolerance were analyzed between different genders. As shown in Table 4, males had higher positive rates for cow's milk and wheat than females ( $P = 0.0059$  and  $0.0444$ , respectively). And the distribution of various food specific IgG levels was also different between males and females with milk and wheat intolerance ( $P = 0.0044$  and  $0.0337$ , respectively) (Table 5).

We then analyzed the association of food intolerance and different ages. The distribution of positive rates with cow's milk, crab, egg, shrimp, tomato and wheat intolerance were all different among the age groups ( $P = 0.0000$ ,  $0.0075$ ,  $0.0000$ ,  $0.03020$ ,  $0.0070$  and  $0.0022$ , respectively) (Table 6). The specific IgG levels in response to these foods among the different age groups were also significantly different ( $P = 0.0001$ ,  $0.0007$ ,  $0.00017$ ,  $0.0389$ ,  $0.0416$  and  $0.0316$ , respectively) (Table 7).

### Discussion

Many studies of food intolerance have been performed world-wide. Food specific circulating IgG detection is now used to provide evidence of a more delayed or even asymptomatic response after exposure to a unique food antigen [10]. In this research, we studied the prevalence of food intolerance in a population with allergic skin diseases in Bengbu, China accord-

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**Table 5.** Correlation of food specific IgG levels and gender

Food	Male (%)			Female (%)			P <sup>s</sup>
	+	++	+++	+	++	+++	
Beef	0.50	0.00	0.00	0.40	0.00	0.00	0.8143
Chicken	1.10	0.50	0.00	2.30	0.00	0.00	0.6151
Codfish	3.30	0.50	0.00	4.60	0.40	0.40	0.4265
Corn	0.50	0.50	0.00	0.00	0.00	0.00	0.0955
Cow's milk	11.80	5.40	4.80	6.50	3.10	2.30	0.0044
Crab	7.50	1.10	0.00	8.10	0.00	0.40	0.9429
Egg	21.00	15.60	15.60	22.40	10.00	18.80	0.9195
Mushroom	2.20	1.10	0.00	2.70	0.80	0.00	0.8985
Pork	0.50	0.00	0.00	2.30	0.40	0.00	0.0920
Rice	5.40	0.00	0.00	1.50	1.20	0.00	0.1554
Shrimp	3.20	0.00	0.00	4.20	0.40	0.40	0.3553
Soybean	9.20	0.50	0.50	11.90	1.90	0.00	0.2472
Tomato	3.80	0.00	1.10	2.70	0.00	0.00	0.2249
Wheat	7.00	0.50	0.00	2.70	0.40	0.00	0.0337

<sup>s</sup>Wilcoxon signed rank test.

**Table 6.** Correlation of food intolerance and age

Food	< 19		19~40		41~59		≥ 60		P <sup>#</sup>
	n	(%)	n	(%)	n	(%)	n	(%)	
Beef	2	1.32	0	0.00	0	0.00	0	0.00	0.2624
Chicken	7	4.64	2	1.17	0	0.00	0	0.00	0.0699
Codfish	11	7.28	5	2.92	5	4.90	0	0.00	0.2607
Corn	1	0.66	0	0.00	1	0.98	0	0.00	0.5640
Cow's milk	54	35.76	15	8.77	3	2.94	0	0.00	0.0000
Crab	8	5.30	12	7.02	12	11.76	6	27.27	0.0075
Egg	105	69.54	72	42.11	45	44.12	8	36.36	0.0000
Mushroom	6	3.97	3	1.75	5	4.90	1	4.55	0.3627
Pork	2	1.32	4	2.34	2	1.96	0	0.00	0.9349
Rice	7	4.64	3	1.75	5	4.90	2	9.09	0.1516
Shrimp	2	1.32	8	4.68	9	8.82	0	0.00	0.0302
Soybean	25	16.56	14	8.19	12	11.76	4	18.18	0.0951
Tomato	9	5.96	2	1.17	2	1.96	3	13.64	0.0070
Wheat	16	10.60	5	2.92	1	0.98	0	0.00	0.0022

<sup>#</sup>Fisher's exact test.

ing to the IgG antibodies against food specific allergens. 66.4% of the population studied was positive for one or more food intolerances, which was higher than the rate previously reported that around 45.8% of middle-aged Chinese in southern (62.3%) and northern China (40.4%) are intolerant to certain foods [11]. Egg intolerance was most common in this population (51.57%) then cow's milk (16.14%), soybean (12.33%), crab (8.52%) and shrimp (6.50%) in order. All patients were divided into four groups according to their age which were <

19, 19~40, 41~59 and ≥ 60 years old, and we found the distribution of food intolerance was different among different age groups but not between genders, which indicates that food intolerance may happen more often in young patients with allergic skin diseases. There was a difference between male and female patients with the distribution of cow's milk and wheat intolerance and levels of cow's milk and wheat specific IgG. Among the different age groups, we observed differences in positive rate distribution of cow's milk, crab, egg, shrimp, tomato and wheat intolerance. Also, various IgG levels in response to the foods were different among the different age groups.

Diagnosis and management of food intolerance in the clinic has been assisted by serologic antibody investigation [12]. The unpleasant symptoms that result from food intolerance include fatigue, abdominal pain, diarrhea, eructation, headache and palpitation after eating certain foods [12]. On the skin rashes, urticaria [3], angioedema [4], dermatitis [5], and eczema [6] can all result. These responses are most often due to enzyme deficiency and vasoactive amines' pharmacological effects. If a food is not completely digested, IgG antibodies may be produced by the body that can develop into immune complexes with food particles resulting in excessive protective immune responses [6].

Cow's milk is one of the most common causes of food intolerance in the first years of life and may also persist in adult patients [13]. One study reported increased levels of milk-specific IgG in children with atopic dermatitis, compared with those of healthy individuals [14]. In this study, we observed the distribution of cow's milk intolerance was different in four age groups and the cow's milk-specific IgG level also showed a difference among these age groups (Table 6). Among all four age groups, 35.76% cow's milk allergy (CMA) patients were

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**Table 7.** Correlation of food specific IgG levels and age

Food	< 19 (%)			19~40 (%)			41~59 (%)			≥ 60 (%)			P <sup>&amp;</sup>
	+	++	+++	+	++	+++	+	++	+++	+	++	+++	
Beef	1.32	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.2707
Chicken	3.97	0.66	0.00	1.17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.0383
Codfish	5.96	1.32	0.00	2.92	0.00	0.00	3.92	0.00	0.98	0.00	0.00	0.00	0.2054
Corn	0.66	0.00	0.00	0.00	0.00	0.00	0.00	0.98	0.00	0.00	0.00	0.00	0.6436
Cow's milk	17.22	9.93	8.61	6.43	1.75	0.58	1.96	0.00	0.98	0.00	0.00	0.00	< .0001
Crab	5.30	0.00	0.00	6.43	0.58	0.00	10.78	0.00	0.98	22.73	4.55	0.00	0.0029
Egg	19.87	20.53	29.14	19.88	7.60	14.62	25.49	9.80	8.82	31.82	4.55	0.00	< .0001
Mushroom	2.65	1.32	0.00	1.17	0.58	0.00	3.92	0.98	0.00	4.55	0.00	0.00	0.5034
Pork	1.32	0.00	0.00	1.75	0.58	0.00	1.96	0.00	0.00	0.00	0.00	0.00	0.8253
Rice	4.64	0.00	0.00	1.17	0.58	0.00	4.90	0.00	0.00	0.00	9.09	0.00	0.2241
Shrimp	1.32	0.00	0.00	4.09	0.58	0.00	7.84	0.00	0.98	0.00	0.00	0.00	0.0239
Soybean	15.23	1.32	0.00	7.02	1.17	0.00	9.80	0.98	0.98	13.64	4.55	0.00	0.1198
Tomato	4.64	0.00	1.32	1.17	0.00	0.00	1.96	0.00	0.00	13.64	0.00	0.00	0.0058
Wheat	9.27	1.32	0.00	2.92	0.00	0.00	0.98	0.00	0.00	0.00	0.00	0.00	0.0009

<sup>&</sup>Kruskal-Wallis test.

under 19 years old. Another study showed high IgG antibodies to  $\alpha$ -lactalbumin in atopic children until 1 year of age and then decreasing antibody levels [15]. Other studies showed similar levels of IgG antibody to cow's milk proteins in healthy individuals and in patients with CMA [16, 17] or low cow's milk-specific IgG levels in CMA patients whether or not tolerance was achieved [18] which may be consistent with our result that only 8.77% and 2.94% patients in group 19~40 and > 40 years.

Other than cow's milk, egg, tomato and wheat intolerance also happened more often in patients under 19 years old. The frequency of Crab and shrimp intolerance was relatively higher in adults, which may because adults eat more sea food like crab and shrimp.

In summary, we studied the prevalence of 14 food intolerances in people with skin allergic diseases in Bengbu, China. We found that food intolerance to cow's milk, egg, wheat and tomato were more likely to happen in children and sea food intolerance such as to crab and shrimp was more likely to happen in adults.

### Disclosure of conflict of interest

None.

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