

# Allergic Risk Among the Children in Southern China: The Association of Influencing Factors with the Allergen Distribution

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**Background:** Due to the inability of children with allergies to exhibit appropriate clinical symptoms, pediatricians often face the challenge of accurately diagnosing allergic diseases in children. Identifying the distribution of allergens is essential for the effective diagnosis and treatment of allergic diseases.

**Methods:** We investigated the distribution of 28 allergens among 12,292 suspected allergic children in Shenzhen, whose serum-specific IgE was subjected to relevance analysis with influencing factors.

**Results:** The results showed the overall allergen distribution was 66.36%. Mite, cow's milk, and egg white were the most prevalent allergens. Indoor allergens are significantly higher than outdoor allergens. There was extensive cross-reactivity among homologous species of allergens such as crustacean allergens, plant-derived allergens, etc. A 14KDa profilin as a common ingredient is suspected to be the main cause of the cross-reactivity among these plant-derived allergens. The frequencies of mite, cow's milk and egg white showed different trends with growing age, indicating that the frequencies of allergens are age-related. Various mechanisms of immune systems of children mature at different ages. We found that the proportion of mite sensitivity was highest in children with allergic rhinitis and conjunctivitis, while the proportion of cow's milk and egg white sensitivity was higher in children with allergic dermatitis such as eczema and urticaria.

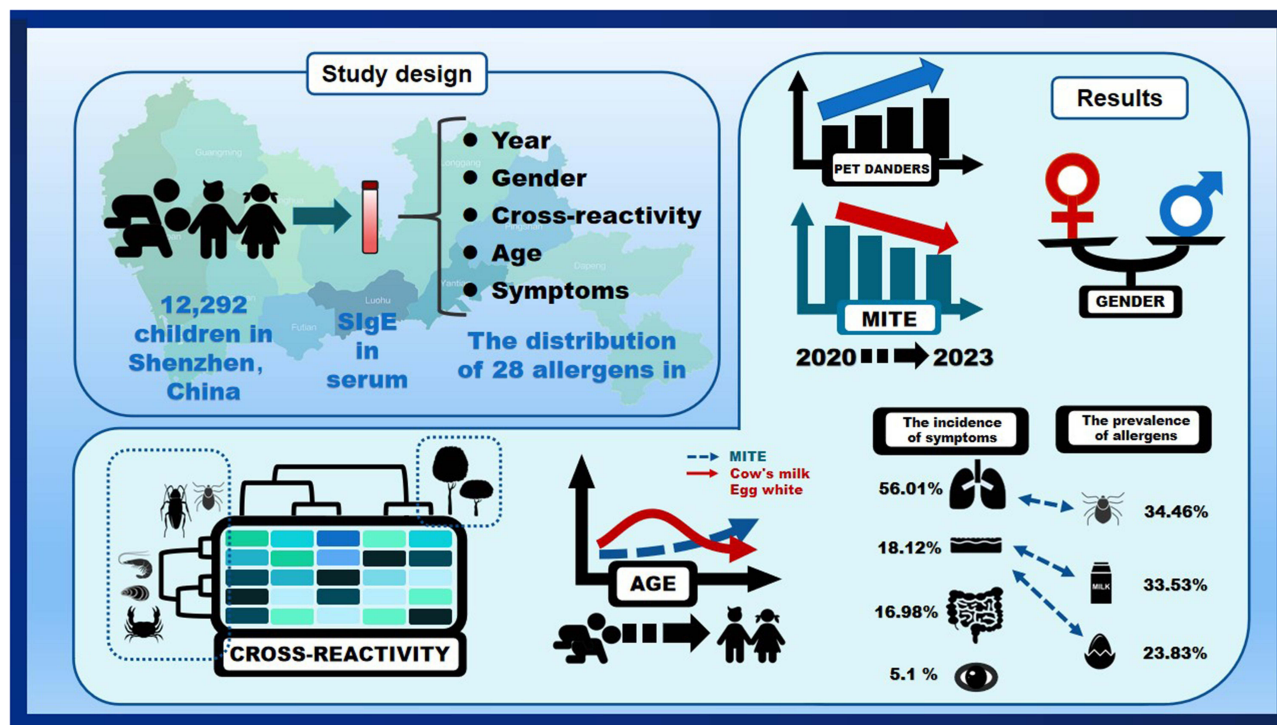
**Conclusion:** Age and cross-reactivity play important roles in diagnosing allergies in children. Children at different ages exhibit varying sensitivities to different types of allergens, and identifying cross-reactions helps to comprehensively understand children's allergic status. Pediatricians can develop corresponding prevention and management measures based on allergen results and clinical symptoms.

**Keywords:** allergen distribution, correlation, cross-reactivity, age, allergic symptoms

## Introduction

Allergic symptoms mediated by specific IgE pose a serious burden on citizen health globally. The number of allergic symptoms diagnosed is growing in all age groups, with pediatric populations demonstrating particularly pronounced epidemiological increase. Allergens are harmless substances that can produce an immune response or an allergic response to a specific population.<sup>1</sup> So far, more than 400 sorts of allergens have been identified, but the characteristics of most allergens are not clear. Common allergens are divided into different groups according to the type of exposure, including food allergens, aeroallergens, and contact allergens. Various clinical symptoms caused by allergens are mainly manifested in respiratory tract, digestive system, and skin. Some allergic patients suffer from skin allergies, eczema, asthma,

## Graphical Abstract



gastrointestinal disorders, even life-threatening diseases such as anaphylactic shock.<sup>2</sup> With the advancement of molecular biotechnology in the detection of allergens, the number of allergen sensitization has been increasing in the past decade. This expansion has produced more comprehensive data that enable systematic analysis of sensitization patterns across diverse demographic, geographic, and environmental contexts.

In recent epidemiology studies, it was considered the prevalence of allergens varies depending on genetic and environmental factors.<sup>3,4</sup> It is also agreed that geographical difference plays a primary role in variability in allergen sensitization.<sup>5</sup> Extensive research has shown that gender and climate variation were also associated with a high risk of allergic diseases.<sup>6</sup> In China, the distribution of allergens with specific symptoms was well investigated in different areas. In theory, allergy vaccination, allergen-specific immunotherapy, and allergen avoidance are accepted as the main treatments applied in the reduction of allergic diseases.<sup>7</sup> However, given its operability, there is no doubt that preventing exposure to potential allergens is the optimal strategy to implement. Therefore, more information regarding allergens is necessary for effective prevention and treatment of allergic diseases. Detailed evidences about risk factors are essential in the analysis of the local allergenic patterns. Here, we made this survey enrolling patients up to seven years of age in Shenzhen and analyzed the relevance of the allergen distribution with various factors as well as corresponding symptoms. Our findings will provide critical insights for developing data-driven prevention strategies targeting pediatric allergic diseases, offering evidence-based recommendations to guide both clinical practice and local public health policies.

## Materials and Methods

### Participants

The study population constituted children with suspected allergies at Longgang District Maternity & Child Healthcare Hospital between 2020 and 2023 in Shenzhen, China. A total of 12,292 children were enrolled in this study including 7126 males and 5166 females. The age range is from 13 days to 7 years old. Based on symptoms, the enrolled patients were tentatively diagnosed with the allergic diseases listed, and whether they are suspected or diagnosed with allergic

diseases by pediatricians according to the diagnostic criteria of World Allergy Organization (WAO) 2020.<sup>8</sup> Exclusion criteria comprised pediatric subjects with recent administration of histamine receptor antagonists, glucocorticoids, or immunosuppressive agents within a 7 days window prior to enrollment, as well as those undergoing anti-allergy therapeutic interventions (eg, anti-IgE monoclonal antibody therapy or allergen-specific immunotherapy) during the 2-month pre-testing period. Written informed consent was diligently obtained from the guardian of the participant contributing to the study. Approval for sample usage was granted by the Ethics Committee of Longgang District Maternity & Child Healthcare Hospital of Shenzhen City (LGFYKYXMLL-2024-96), and the study was conducted in accordance with the Declaration of Helsinki.

## Detection Methods

All of the patients enrolled in this study underwent serum-specific IgE measures. Five milliliters of venous blood samples were extracted, separated using vacuum coagulation tubes, and centrifuged at 3000 rpm for 10 minutes. The upper serum was collected to test for 28 sorts of allergens as follows: amaranth, beef, cashew, cat dander, chaff, cockroach, cod, cow's milk, crab, dog dander, egg white, felon herb, house dust, lobster, mango, mite, mould, mulberry, mutton, peanut, pineapple, pollen, ragweed, salmon, scandent hop, shellfish, shrimp, soy. The concentrations of 28 allergen-specific IgE in serum were quantitatively measured using an indirect chemiluminescent immunoassay (CLIA). The levels (LV) of allergens concentrations were cataloged according to the following standards: LV0 [0.00–0.34 IU/mL], LV1 [0.35–0.69 IU/mL], LV2 [0.70–3.49 IU/mL], LV3 [3.50–17.50 IU/mL], LV4 [17.50–49.99 IU/mL], LV5 [50.00–100.00 IU/mL], LV6 [ $>100.00$  IU/mL]. Specific IgE levels exceeding 0.35 IU/mL were defined as positive.

## Statistical Analysis

R version 4.3.2 was used for data analysis and visualization of the results. The correlation between the 28 allergens was analyzed using Spearman correlation.  $p < 0.05$  was considered as a statistically significant difference.

## Results

### Epidemiological Characteristics of Allergen Distribution

A total of 12,292 children with suspected symptoms caused by allergic reasons were selected. The age distribution in the study population is shown in Table 1. The clinical manifestations mainly included four types (Figure 1A). The main symptoms were concentrated in the respiratory tract (56.01%), including rhinitis, chronic cough, and asthma, etc. More

**Table 1** The Age Distribution of the Study Population and the Positive Rates of 28 Allergen in Each Age Group

Age group	< 1 year	1 year	2 years	3 years	4 years	5 years	6 years	7 years
N (%)	1753 (14.26)	2118 (17.23)	1652 (13.44)	2326 (18.92)	1923 (15.64)	1264 (10.28)	760 (6.18)	496 (4.04)
Food allergen (n, n/N)								
Peanut	32 (1.83)	61 (2.88)	63 (3.81)	92 (3.96)	63 (3.28)	33 (2.61)	22 (2.89)	15 (3.02)
Soy	22 (1.25)	37 (1.75)	42 (2.54)	52 (2.24)	36 (1.87)	21 (1.66)	15 (1.97)	6 (1.21)
Lobster	22 (1.26)	76 (3.59)	70 (4.28)	87 (3.74)	54 (2.81)	47 (3.72)	31 (4.08)	25 (5.04)
Salmon	4 (0.23)	7 (0.33)	3 (0.18)	10 (0.43)	7 (0.36)	2 (0.16)	5 (0.66)	3 (0.60)
Cod	3 (0.17)	13 (0.61)	17 (1.03)	29 (1.25)	25 (1.30)	12 (0.95)	7 (0.92)	5 (1.01)
Mutton	3 (0.17)	3 (0.14)	3 (0.18)	5 (0.21)	4 (0.21)	7 (0.55)	4 (0.53)	3 (0.60)
Pineapple	3 (0.17)	1 (0.05)	0 (0)	1 (0.04)	1 (0.05)	1 (0.08)	3 (0.39)	1 (0.20)
Cashew	22 (1.25)	63 (2.97)	54 (3.27)	101 (4.34)	66 (3.43)	34 (2.69)	19 (2.50)	15 (3.02)

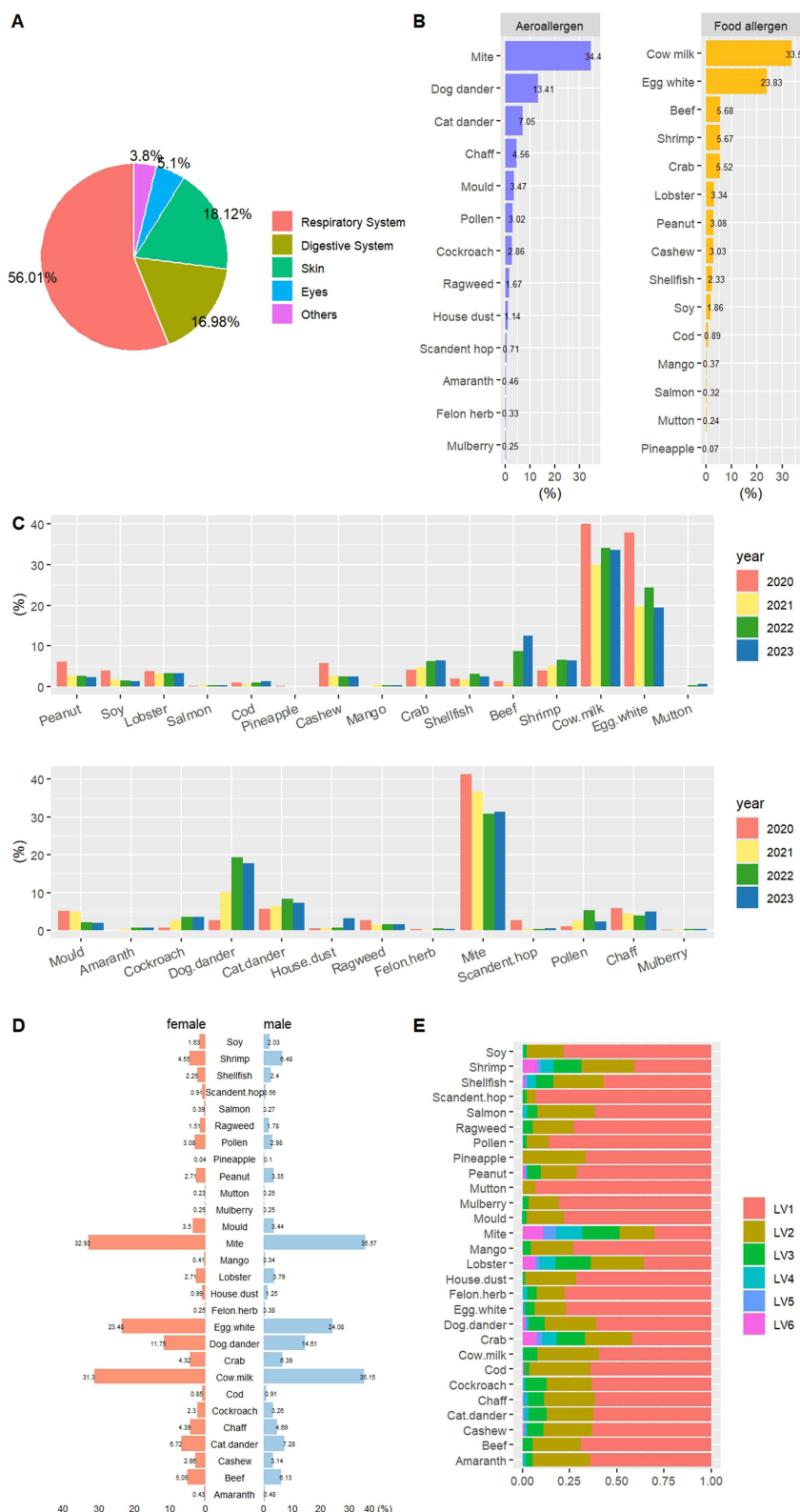
(Continued)

**Table 1** (Continued).

Age group	< 1 year	1 year	2 years	3 years	4 years	5 years	6 years	7 years
Mango	3 (0.17)	2 (0.09)	4 (0.24)	12 (0.52)	11 (0.57)	11 (0.87)	2 (0.26)	2 (0.40)
Crab	40 (2.28)	128 (6.04)	137 (8.29)	133 (5.72)	91 (4.73)	66 (5.22)	49 (6.45)	36 (7.26)
Shellfish	12 (0.68)	33 (1.56)	35 (2.12)	66 (2.84)	55 (2.86)	38 (3.01)	23 (3.03)	26 (5.24)
Beef	44 (2.51)	102 (4.82)	118 (7.14)	150 (6.45)	113 (5.88)	79 (6.25)	56 (7.37)	38 (7.66)
Shrimp	41 (2.34)	135 (6.37)	141 (8.54)	139 (5.98)	92 (4.78)	66 (5.22)	47 (6.18)	38 (7.66)
Cow's milk	482 (27.50)	774 (36.54)	633 (38.32)	847 (36.41)	652 (33.91)	396 (31.33)	213 (28.03)	127 (25.61)
Egg white	383 (21.85)	645 (30.45)	497 (30.08)	600 (25.80)	397 (20.64)	227 (17.96)	113 (14.87)	69 (13.91)
Aeroallergen (n, n/N)								
Amaranth	1 (0.06)	3 (0.14)	1 (0.06)	12 (0.52)	10 (0.52)	13 (1.03)	8 (1.05)	2 (0.40)
Cockroach	5 (0.29)	13 (0.61)	34 (2.06)	75 (3.22)	63 (3.28)	69 (5.46)	54 (7.11)	41 (8.27)
Dog dander	159 (9.07)	320 (15.11)	288 (17.43)	331 (14.23)	249 (12.95)	148 (11.71)	90 (11.84)	65 (13.10)
Cat dander	50 (2.85)	145 (6.85)	134 (8.11)	177 (7.61)	152 (7.90)	100 (7.91)	69 (9.08)	41 (8.27)
Mulberry	0 (0)	2 (0.09)	3 (0.18)	8 (0.34)	8 (0.42)	6 (0.47)	4 (0.53)	2 (0.40)
House dust	2 (0.11)	2 (0.09)	8 (0.48)	16 (0.69)	29 (1.51)	27 (2.14)	27 (3.55)	32 (6.45)
Mould	24 (1.37)	56 (2.64)	61 (3.69)	108 (4.64)	71 (3.69)	59 (4.67)	31 (4.08)	19 (3.83)
Ragweed	8 (0.46)	17 (0.80)	35 (2.12)	53 (2.28)	38 (1.98)	31 (2.45)	16 (2.11)	9 (1.81)
Felon herb	2 (0.11)	9 (0.42)	4 (0.24)	8 (0.34)	7 (0.36)	8 (0.63)	6 (0.79)	2 (0.40)
Mite	166 (9.47)	324 (15.30)	550 (33.29)	964 (41.44)	909 (47.27)	640 (50.63)	397 (52.24)	288 (58.06)
Scandent hop	9 (0.51)	9 (0.42)	14 (0.84)	17 (0.73)	15 (0.78)	11 (0.87)	8 (1.05)	6 (1.21)
Pollen	28 (1.60)	52 (2.46)	57 (3.45)	74 (3.18)	63 (3.28)	42 (3.32)	38 (5.00)	19 (3.83)
Chaff	28 (1.60)	92 (4.34)	85 (5.15)	131 (5.63)	94 (4.89)	59 (4.67)	46 (6.05)	28 (5.65)

than 18% of children developed skin allergies, 1043 cases of children were confirmed as eczema; 980 children suffered from urticaria. Within the study cohort, digestive system diagnoses (including abdominal pain, diarrhea, and dyspepsia) accounted for 16.98% of all clinical manifestations. Specific IgE antibodies in serum were performed to detect the allergens. The degree of the allergen sensitization was measured by concentration of IgE. The positive rate of the overall samples was 66.36%, indicating that 8154 of 12,292 children in this study were sensitive to at least one allergen. Over one-third of children were sensitive to cow's milk (33.53%, 4122/12292), followed by egg white (23.83%, 2929/12292). The first three allergens in aeroallergen were mite (34.46%, 4236/12292), dog dander (13.41%, 1648/12292), and cat dander (7.05%, 866/12292), and the percentage of other allergens were less than 6%, ranging from 0.07% to 5.68% (Figure 1B). The positive rate of each allergens related with age distribution is presented in Table 1.

The trends of the positive rates in various allergens from 2020 to 2023 are shown as Figure 1C. In the food allergens, the positive rates of peanut, soy, cashew, cow's milk, and egg white reached the high points in 2020 and then declined sharply in the next three years. On the contrary, crab and shrimp showed a gradual upward trend from 2020 to 2023, and the positive rate of beef increased significantly from 2022. In aeroallergen, the sensitivity of mite revealed a downward trend, while the sensitivities of cat and dog dander showed an upward trend. We also compared the differences among



**Figure I** Characteristics of allergen distribution. **(A)** The incidence of diagnosis in children with suspected symptoms caused by allergenic reasons. **(B)** The overall frequencies of 28 allergens. **(C)** The changes in allergens from 2020 to 2023. **(D)** The frequencies of allergens between genders. **(E)** The distribution of sensitivity levels to various allergens.

participants of different genders and found the positive rates of various allergens in different genders were exactly the same (Figure 1D).

In addition to single allergen sensitivity children, 4787 children were sensitive to two or more allergens, and the positive rate of the children with multiple sensitivities was 38.94%. While the majority of allergen-specific positive rates exhibited a decline with increasing sensitization severity, notable exceptions were observed for crustaceans (eg, lobster, crab, shrimp), cashew, egg white, dog dander, mite, and chaff, where positive rates of sensitization were significantly elevated at LV 6 sensitization compared to LV 5 (Figure 1E).

### Correlation Among Multiple Allergenic Sensitization

Spearman correlation analysis was used to analyze the relationship between individual allergens, and the clustering method was the K-means clustering algorithm. The strongly positive correlations mainly were concentrated in four areas (Figure 2). Firstly, there was a significant positive correlation among crustacean, and the correlation between crab and shrimp was the strongest ( $r = 0.96, p < 0.001$ ). Cockroach was positively correlated with shellfish ( $r = 0.37, p < 0.001$ ), lobster ( $r = 0.33, p < 0.001$ ), crab ( $r = 0.28, p < 0.001$ ) and shrimp ( $r = 0.29, p < 0.001$ ). The second significant positive correlation has appeared in the cluster which contains aeroallergen and mango. Mango is generally a food allergen but is also regarded as a contact allergen, which is related to amaranth ( $r = 0.44, p < 0.001$ ), mulberry ( $r = 0.51, p < 0.001$ ), and felon herb ( $r = 0.49, p < 0.001$ ). Despite the frequency of amaranth was as low as 0.46%, it was detected to be significantly positively correlated with up to six allergens. We attempted to investigate the allergenic ingredient from the website of ALLERGEN NOMENCLATURE ([www.allergen.org](http://www.allergen.org)), and found profilin with a molecular weight of 14KDa was a common part of amaranth, mango, and ragweed (Table 2). Profilin was not retrieved in mulberry, but non-specific lipid transfer protein type 1 (nsLTP1) with molecular weights ranging from 10 to 15 KDa were retrieved. In addition, no

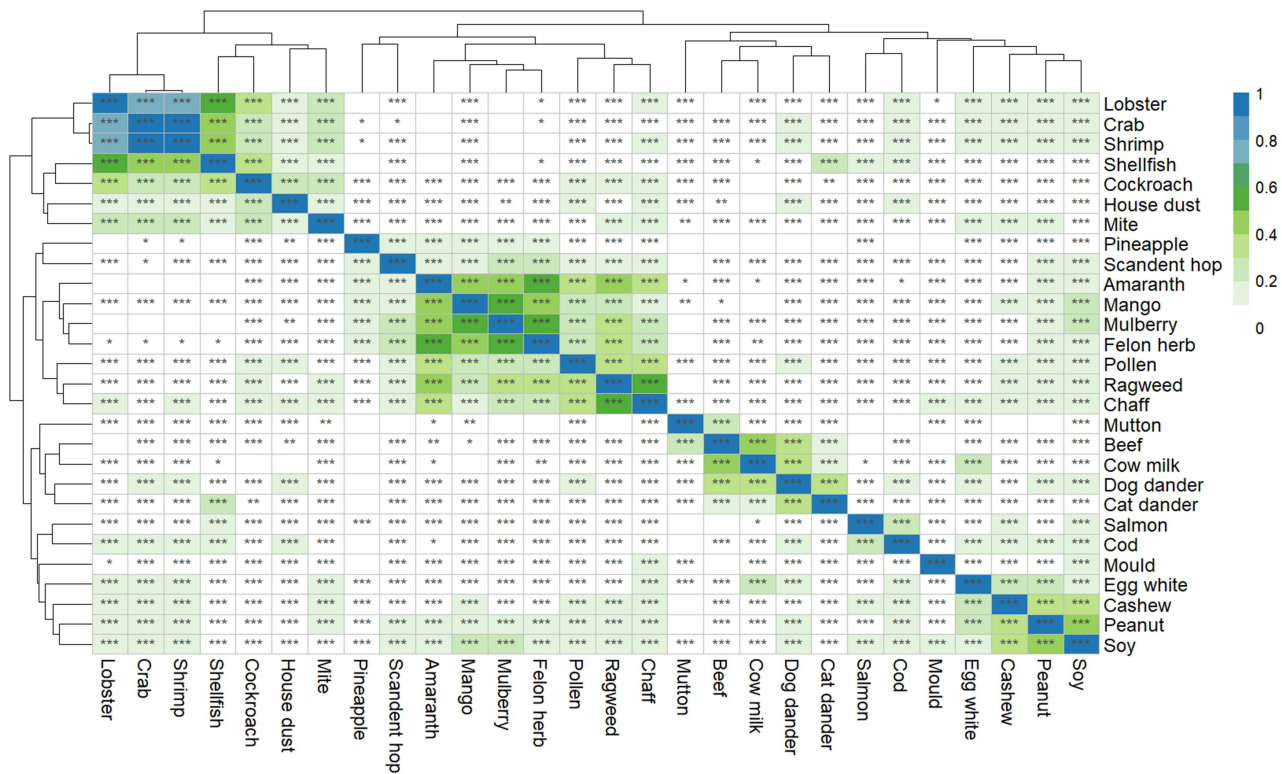


Figure 2 Spearman correlation between 28 allergens. (\*p < 0.05; \*\*p < 0.01; \*\*\*p < 0.001).

**Table 2** The Allergenic Ingredients of Plant-Related Allergens

Species	Allergen	Biochemical Name	MW	Route of Allergen Exposure
Amaranth	Amar 1	Ole e l- like protein	18 kDa	Airway
	Amar 2	Profilin	14 kDa	Airway
Mango	Man i 1	Class IV chitinase	28 kDa	Food
	Man i 2	PR-10 protein; Bet v l-related protein	17 kDa	Food
	Man i 4	Profilin	14 kDa	Food
Ragweed	Amb t 5	Profilin	5 kDa	Airway
	Amb t 8		14 kDa	Airway
	Amb t 13	Superoxide dismutase	17 kDa	Airway
	Amb t 18	Triosephosphate isomerase	26 kDa	Airway
Mulberry	Bro p 3/ Mor n 3	Non-specific lipid transfer protein class I (nsLTP1)	10–15 kDa	Airway/Food

research results were found in felon herb, chaff, and pollen due to diversity in species naming. Beef was positively correlated with milk ( $r = 0.42$ ,  $p < 0.001$ ), and the correlations among cashew, peanut, and soy were also found.

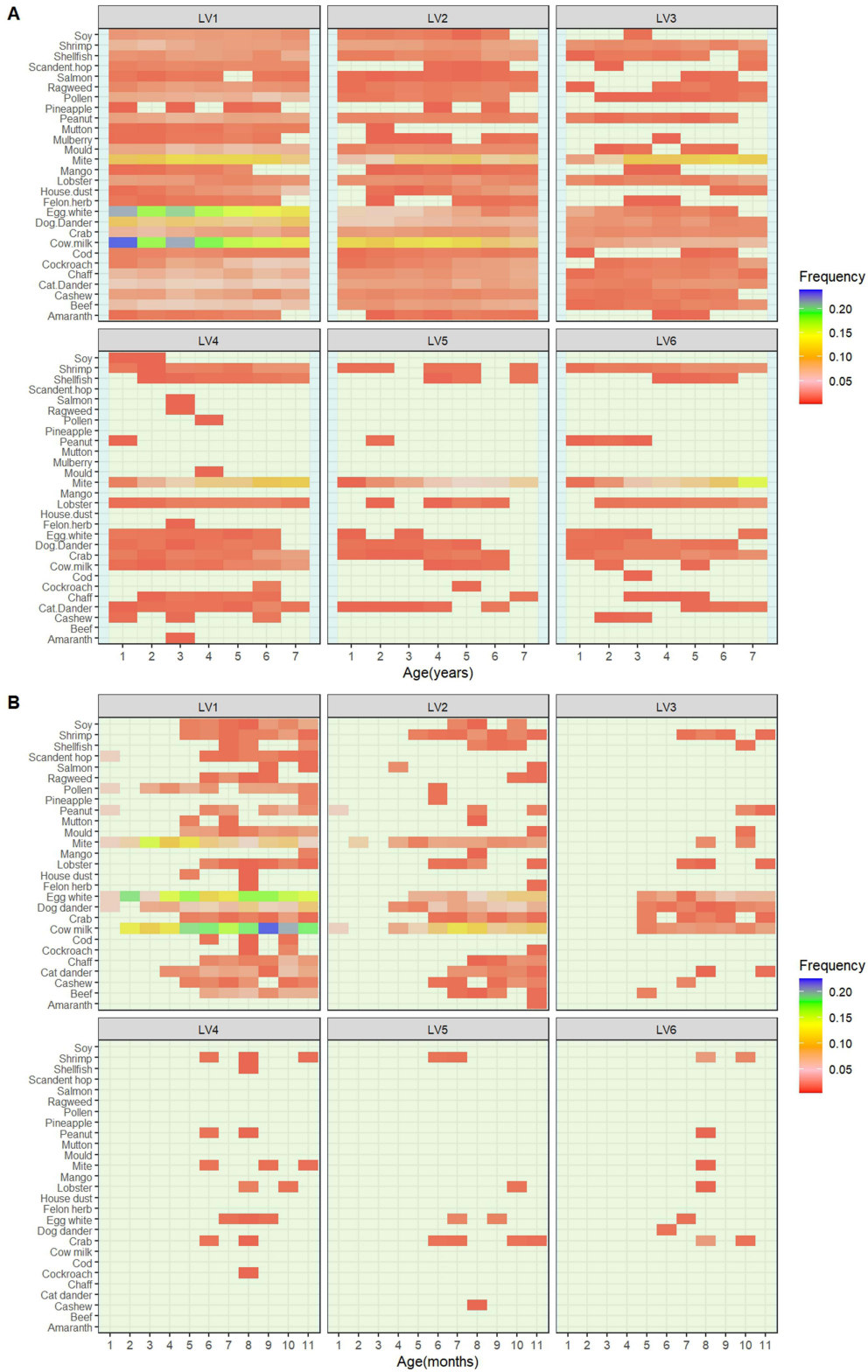
## The Risk of Allergy in Children Was Age-Related

It was universally acknowledged that allergic sensitization first occurs in early childhood. We explored the relationship of the age with the allergen frequencies in the allergic population under seven years. According to the age and the degree of sensitivity, all the results of the serum IgE concentration were classified and described in [Figure 3A](#), the frequencies of the allergens were determined to be age-related. The mite allergen exhibited the highest positive rate among all tested allergens and was consistently prevalent across all age groups. Its frequency demonstrated an age-dependent increase, although the variation of sensitivity at LV1 remained statistically insignificant. Egg white and milk allergens showed a downward trend, the positive rate was high in the early stage, and then gradually decreased.

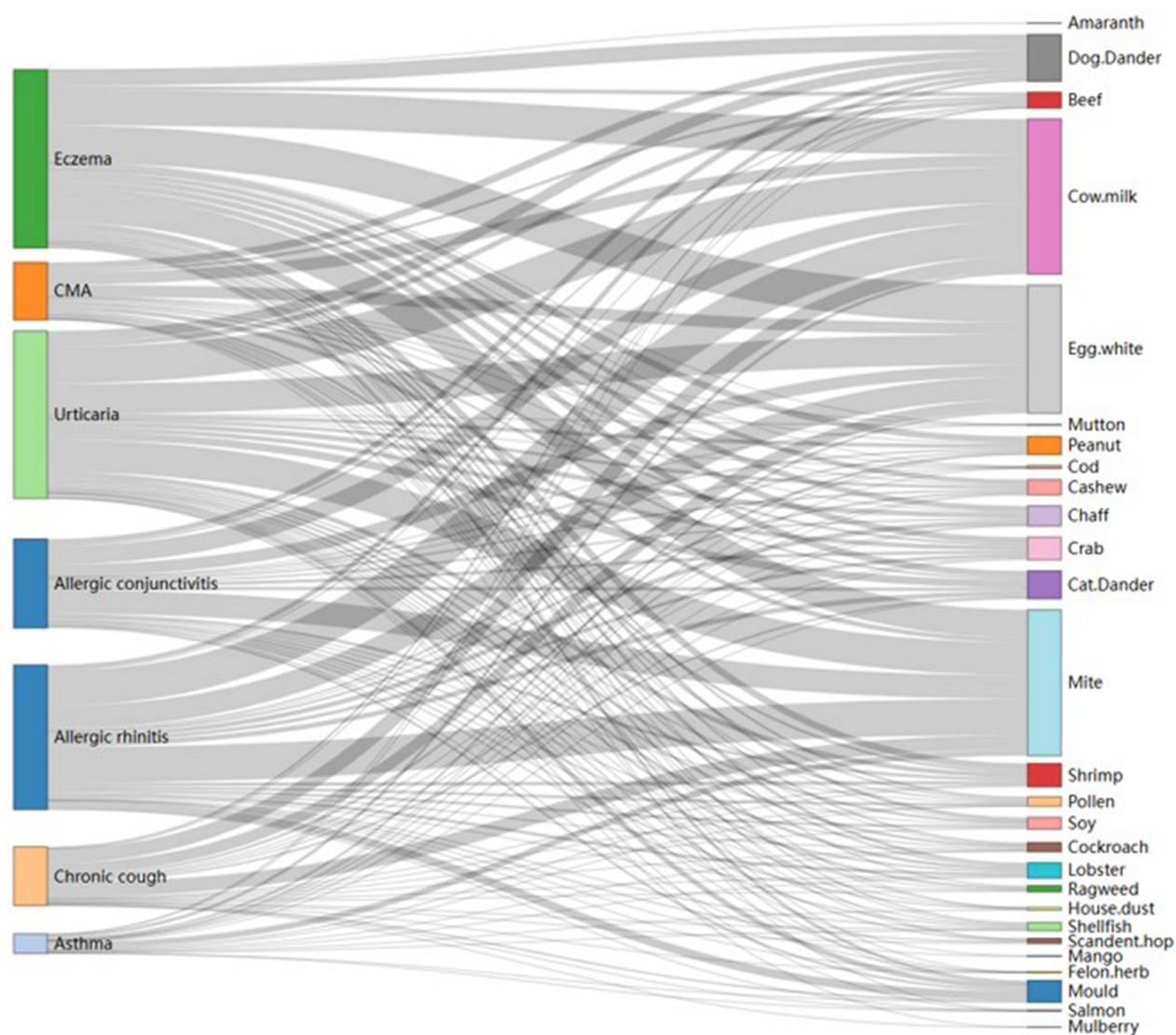
It was also necessary to confirm whether this allergic sensitization occurs within the first year of life, and more evidence is needed to explain at which stage allergic sensitization occurs. Here, we next investigated the frequencies of allergenic sensitization in infants under one year old. It was seen that the majority of allergens were detected five or six months after birth ([Figure 3B](#)). In the first four months, there were only a few types of allergens that could be detected, including aeroallergens such as mite, dog dander, scandent hop, and pollen, and food allergens such as milk, egg, and peanut. The chart also shows that the frequencies of milk and egg white allergens increase with age.

## The Sources of Allergens in Different Allergic Symptoms

The allergen results of 4185 participants with confirmed symptoms were selected. The pairwise relation between different allergens and main allergic symptoms was drawn as Sankey diagram ([Figure 4](#)). The main allergens of eczema were derived from egg white (219/1043, 21.00%), cow's milk (19.85%, 207/1043) and mite (15.72%, 164/1043); in urticaria, the top three allergens were cow's milk (21.84%, 214/980), mite (19.48%, 191/178) and egg white (18.16%, 178/980); The proportion of mites in allergic rhinitis and conjunctivitis was the highest, 24.97% (211/845) and 26.73% (139/520), respectively. The proportion of mould in allergic rhinitis was very noteworthy at 5.91% (50/845) because most of the patients with allergic to mould were confirmed as having rhinitis (39.37%, 50/127). Allergic conjunctivitis was frequently observed in house dust-positive patients, with a prevalence rate of 56.25% (9/16). The proportion of patients diagnosed with cow's milk allergy (CMA) who are positive for milk allergens was 21.07% (71/337), followed by egg white (20.47%, 69/337) and dog dander (12.76%, 43/337).



**Figure 3** The relationship between allergen frequencies and age. **(A)** The frequencies of allergens in children aged 1 to 7 varies with age. **(B)** The frequencies of allergens in children under 1 year old varies with age.



**Figure 4** The pairwise relation between different allergens and the allergic symptoms.  
**Abbreviation:** CMA, Cow's milk allergy.

## Discussion

This retrospective study among 12,292 suspected allergic children in Shenzhen, China, produced the most precise and representative data of 28 allergens. The prevalence of the total allergens in our study was 66.36%, demonstrating more than half of the participants were at risk of allergies. Despite different definitions of the participants enrolled, the total positive rate demonstrate concordance with other epidemiological investigation conducted in southern China, wherein 65.97% of 6689 allergic rhinitis patients exhibited allergen sensitization,<sup>9</sup> But similar to other studies, the most popular aeroallergen was indoor allergen including mite, dog dander, and cat dander, the sensitivity frequencies of which are more higher than other outdoor allergens.<sup>10</sup> On the other hand, cow's milk and eggs were found as the most common food allergens with high frequencies. Cow's milk has been the main source of nutrition for children, especially for infants with breastfeeding difficulties.<sup>11</sup> Children who are allergic to cow's milk always show eczema, gastrointestinal discomfort, or other symptoms. In order to solve this problem, it is generally recommended to use widely hydrolyzed formulas and amino-acid-based formulas as alternatives to relieve severe skin or intestinal symptoms.<sup>12</sup> Another important finding is the annual variation in positive rates. The observed reduction in mite infestation rates within

residential settings during China's COVID-19 containment phase (2020–2022) demonstrates a significant correlation with enhanced public adherence to indoor hygiene protocols and intensified sanitation measures. During the same period, China was faced with the serious problems of low fertility and declining birth rate. Most young people prefer to keep pets rather than get married, which leads to an increase in the prevalence of pet dander allergens.

Accurately diagnosing allergic diseases in children is difficult. While controlling symptoms and reducing inflammation are common treatment approaches, avoiding potential allergens is the most effective strategy for preventing the onset of allergic diseases in this population. To implement this strategy effectively, it is essential to gather comprehensive information about pediatric patients, including the collection of specific IgE biomarkers for molecular allergens. This process also involves eliminating cross-reactions caused by pan-allergens to accurately genuine sensitization. In the correlation analysis, there was a significant positive correlation between milk and beef, indicating that there was a source of cross-reactive allergens between them. The epidemiological survey in 2002 confirmed that more than 90% of children with milk allergy were also allergic to beef.<sup>13</sup> Another cross-reaction occurred in crustacean such as lobster, crab, shrimp, and shellfish, and the correlation between shrimp and crab was the strongest. Salmon and cod are marine products but have no significant correlation with crustacean. Cockroach was observed to be involved in this cluster of crustacean. The cross-reactivity between cockroach and shrimp was consistent with the results from serum-specific IgE measurement in a previous study, which is also considered to be the explanation of the high-sensitivity frequency of shrimps in low shrimp consumption areas.<sup>14,15</sup> Tropomyosin in shrimp is a muscle contraction protein documented commonly in arthropods, with primary IgE sensitization in 70% of all shellfish allergies.<sup>16</sup> In recent studies, tropomyosin was considered a cross-reactive source between house dust mite and shrimp, the phenomenon of which was also detected in our study.<sup>17,18</sup> However, tropomyosin was not confirmed as a major allergen relevant to the cross-reactivity between shrimp and cockroach.<sup>15</sup> Alternatively, the largest cluster by correlation analysis in this study was entirely composed of plant-derived antigens. In the epidemiological analysis, allergic reactions to members of this group were extremely rare. The incidences were less than 5%. Amaranth had cross-reactions with six sorts of allergens, but it was easy to ignore due to its low prevalence. A 14KDa profilin was isolated from amaranth, mango, and ragweed, which may be the main source of cross-reaction of these plant-derived allergens. Profilin plays a significant role in the cross-reactivity between pollen and plant-derived foods. The expression of Bet v1 and Bet v2 (birch profilin) in pollen is highly upregulated, particularly during the maturation period of pollen. Despite the low content of these proteins in the plant tissue cells, pollen is still regarded as the primary allergen for pollen-food allergic sufferers.<sup>19</sup> The patients allergic to pollen frequently exhibit allergic symptoms when consuming plant-derived foods, which is attributed to the cross-reactivity of IgE antibodies with conserved plant allergens. Research has demonstrated that profilin also functions as an allergen in plant-derived foods like mango, exhibiting cross-reactivity with other pollen allergens.<sup>20,21</sup> However, more experimental evidence about profilin in amaranth is needed.

There is a consensus that the clinical symptoms of anaphylaxis are closely related to age. One multi-central research covering four southern China cities was performed between 2007 and 2019, it was found that the different types of antigens showed different tendencies with the growth of age. From childhood to adulthood, the positive rate of aeroallergens such as mite showed a downward trend which should be attributed to the improvement of immunity in the respiratory system as growing age.<sup>22</sup> However, the changes of allergen sensitivity in childhood are rarely reported. The whole childhood is divided into two parts: infant (0–1 year) and preschool (1–7 years). In preschool children, the positive rate of mites showed an upward trend, especially in LV3-6. Compared with the adult stage, the changing trend of mite positive rate at this stage is opposite, indicating that children's respiratory immune system is difficult to adapt to mite sensitization before school age. The positive rates of cow's milk and egg white in preschool children were basically the same, showing a downward trend, and the positive rates of LV1 and LV2 were the highest. In contrast, it is easy to see that the positive rate of cow's milk in infants is rising. One possible explanation may be that the infant's immune system adapts to cow's milk differently from the mites discussed above. The adaptive capacity of the intestinal immune system matures around the age of one.<sup>23</sup> For infants, it is more important to detect the low concentration of cow's milk IgE than preschool children, because they are more prone to suffer from pruritus and even eczema. It is worth noticing that the allergens to peanut and egg, which were found in the first four months of the infant feeding phase, should not be included as a component of infant nutrition during this period, as these immunoreactive components were most likely transferred

via breast milk following maternal dietary intake. Therefore, breastfeeding is one of the important methods to reduce the occurrence of food allergies, but the safety of allergens in breast milk can not be ignored.<sup>24</sup>

It is generally believed that children do not need routine allergen screening unless they have repeated allergic reactions. However, children can not show allergic symptoms well, and pediatricians often have difficulties in correctly identifying these symptoms, so it is difficult to diagnose allergic reactions in children. It is suggested that serum IgE can provide an experimental basis for pediatricians to diagnose CMA. Twenty-one percent of CMA children were antibody positive, which could be consistent with the statistical data of non-IgE mediated CMA (56.3–73%), and the allergen source of allergic diseases could also be determined by serum IgE. Allergens of allergic skin diseases in children such as eczema and urticaria mainly come from egg white and milk, while allergens of chronic cough, allergic rhinitis, and allergic conjunctivitis mainly come from mites. Allergic rhinitis is considered to have a close epidemiological relationship with allergic conjunctivitis due to its similar pathophysiological mechanism.<sup>25</sup>

## Conclusions

We conducted a thorough analysis of allergen sensitivity among suspected allergic children in southern China. Our findings revealed that the positive rates of the mites, cow's milk, and egg white were the highest among the 28 allergens tested, with significant cross-reactions observed between cockroach allergens and crustaceans, such as shrimp and crab. Similar cross-reactions were noted among plant-derived allergens as well. Cow's milk and egg white emerged as the primary allergens associated with skin conditions like eczema and urticaria in children. Notably, the sensitivity to cow's milk and egg white in children under seven years old exhibited a clear age-related, displaying an inverted U-shaped trend with age, peaking around one year old. Therefore, when diagnosing allergic diseases in children, it is crucial to consider various factors, including the patient's age, potential cross-reactions, clinical symptoms, allergic history, and other relevant details. The results of this study can provide valuable guidance for the feeding of infants and the prevention of allergic diseases in this region.

## Abbreviations

LV, Level; nsLTP, non-specific lipid transfer protein; CMA, Cow's milk allergy.

## Data Sharing Statement

The data in this study is available from the corresponding author on reasonable request.

## Ethics Approval and Informed Consent

Approval for sample usage was granted by the Ethics Committee of Longgang District Maternity & Child Healthcare Hospital of Shenzhen City (LGFYKYXMLL-2024-96). Written informed consent was diligently obtained from the guardian of the participant contributing to the study.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare no competing interests in this work.

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