

## Food allergy in nursery children of Kawasaki city, Japan

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### Abstract

**Background:** Food allergies are often life threatening. In order to establish appropriate food allergy measures in nursery children, it is important to analyze local epidemiological data on the food allergy prevalence in nursery children. However, no such data are currently available for the city of Kawasaki, Japan.

**Objective:** The present study retrospectively evaluated food allergy prevalence among nursery children in Kawasaki city.

**Methods:** Data from children with food allergies requiring food avoidance in the nurseries of Kawasaki city between 2007 and 2016 were evaluated.

**Results:** From 2007 to 2016, the prevalence of food allergies among nursery children in Kawasaki city increased from 2.7% to 5.3%. The increase of food allergy prevalence was higher in 2–5 year-old children than in 0–1 year-old children (2.0% to 4.7% vs. 5.3% to 7.0%, respectively). The top five most common food allergies were hen's egg (73.0%), cow's milk (29.3%), nuts (9.7%), soy (8.9%), and wheat (6.5%). Hen's egg was consistently identified as a causative food of food allergy in more than 70% (73.0–89.1%) of food avoidance cases over the 10 year period. The increase of egg allergy prevalence was higher in 2–5 year-old children than in 0–1 year-old children (1.7% to 3.2% vs. 5.2% to 6.0%, respectively).

**Conclusions:** Food allergies, to hen's egg in particular, have increased considerably among nursery children in the city of Kawasaki, Japan, and that increase was higher among older children.

**Key words:** Food allergy, Egg allergy, Prevalence, Food avoidance, Epidemiology, Tolerance, Japan, Nursery

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### Background

Food allergy is a life-altering disease, which is often life threatening.<sup>1</sup> Its management entails dietary avoidance of the identified allergen, thus preventing allergic reactions.<sup>2</sup> An adequate management of nursery children with food allergy is particularly important, given the possibility of accidental ingestion of culprit foods. Therefore, strict care is required for children with food allergies, to avoid allergic reactions that can lead to a fatal condition such as life-threatening anaphylaxis.

Kawasaki city, Japan, is located next to the capital city Tokyo, and its population is over 1,500,000. Among its residents, the demand for nurseries is very high. The Kawasaki city office

has authorized the nurseries to administer the health and safety of nursery children. Since 1995, all nurseries authorized by the Kawasaki city office have managed children with food allergies requiring food avoidance who are registered with certification by their primary care doctors. This measure aims to confirm the medical information of allergic nursery children in order to safely manage their nursery life while preventing allergy-related life-threatening incidents. Such management allows all authorized nurseries in Kawasaki city to recognize every single child with food allergy requiring food avoidance, therefore providing appropriate care, even if they are at risk of life-threatening anaphylaxis.

The nursery administration department in the Kawasaki city office has teamed up with the Kawasaki branch of the Japan medical association to run the health administration committee of nursery in Kawasaki city. The committee has required all families with allergic children requiring food avoidance to submit certification by primary care doctors confirming that requirement. Registered allergic children have been followed and managed by nurseries, and the need for food avoidance has been regularly overlooked by primary care doctors.

Data regarding the local epidemiology of allergic diseases are vital to support evidence-based prevention and management strategies. In particular, the prevalence of food allergies in nursery children can be significant to establish their appropriate management. However, no local epidemiological data on food allergy in nursery children are currently available for the city of Kawasaki, Japan.

Our study aimed to identify the prevalence of food allergy in the nurseries of Kawasaki city, Japan, in order to evaluate its impact, observing how its prevalence changes over time.

## Methods

### Study design

This retrospective study was conducted to analyze the data from children registered as food allergies requiring food avoidance at nurseries in Kawasaki city, from 2007 to 2016.

Food allergy children were defined with certification by their primary care doctors who diagnosed them and classified them as requiring food avoidance.

This study aimed to identify the prevalence of food allergy in nursery children of Kawasaki city.

This study was approved by the Institutional Review Board of The Department of Nursery Health Administration, Kawasaki Branch of the Japan Medical Association. Given the retrospective nature of the study, the participants' informed consent was not required.

### Data collection

The doctors' certifications of all children with food allergy requiring food avoidance were submitted to the nursery through their families. The health administration committee of nursery in Kawasaki city has gathered the doctors' certifications of authorized nurseries in each year.

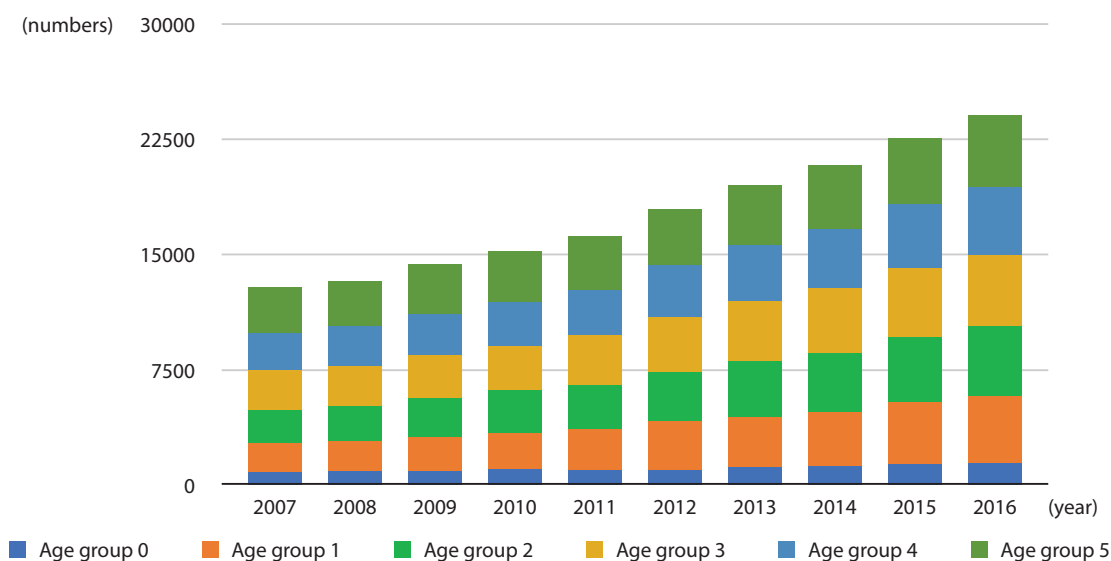
### Statistical analysis

Statistical analysis was performed using js-STAR version 9.1.8j (<http://www.kisnet.or.jp/nappa/software/star/index.htm>). The chi-square test was used to compare the proportion of categorical variables between the groups. The threshold for significance was  $P < 0.05$ .

## Results

The number of nursery children in Kawasaki city, Japan, increased considerably from 12,729 in 2007 to 23,969 in 2016, whereas the age distribution among nurseries showed unremarkable changes (Figure 1). Food allergy children in the nurseries increased significantly from 2.7% to 5.3% ( $P < 0.01$ ) (Figure 2).

The prevalence of food allergies was analyzed by age for six groups: age group 0 (0- < 1 years old), age group 1 (1- < 2 years old), age group 2 (2- < 3 years old), age group 3 (3- < 4 years old), age group 4 (4- < 5 years old), and age group 5 (5- < 6 years old). The results showed clear differences among ages regarding the prevalence of food allergy (Figure 3), with the highest prevalence observed in age group 0 and 1, followed by age group 2, 3, 4, and 5. Comparing the prevalence of food allergy between 2007 and 2016, no significant increase was found in age group 0, who presented 4.6% prevalence in both 2007 and 2016. On the other hand, age group 1, 2, 3, 4, and 5 showed an increase in the prevalence of food allergy from 5.5% to 7.7%, 3.6% to 7.0%, 2.4% to 5.0%, 1.4% to 4.0%, and 1.1% to 3.0%, respectively. Although a relatively



**Figure 1. The total number and age distribution of nursery children in Kawasaki city from 2007 to 2016.** Age group 0; < 1 years old, Age group 1; 1- < 2 years old, Age group 2; 2- < 3 years old, Age group 3; 3- < 4 years old, Age group 4; 4- < 5 years old, Age group 5; 5- < 6 years old

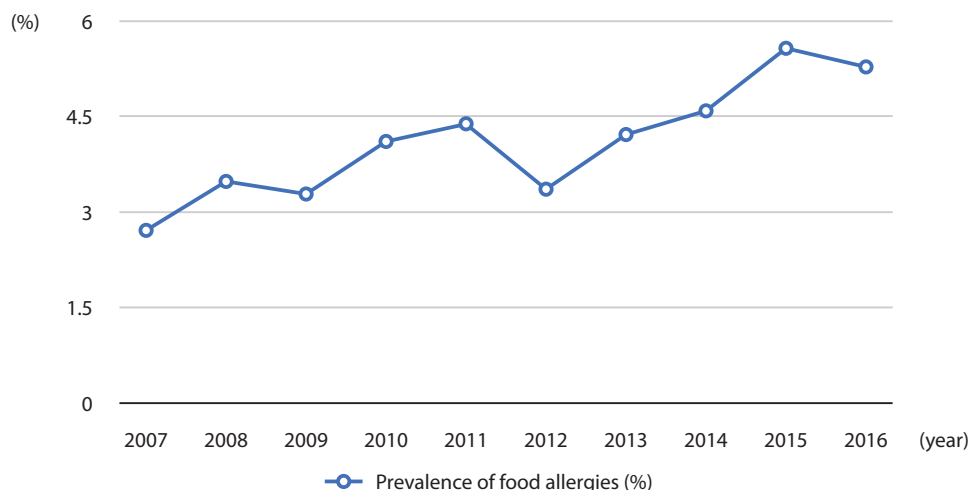


Figure 2. Prevalence of food allergies among nursery children.

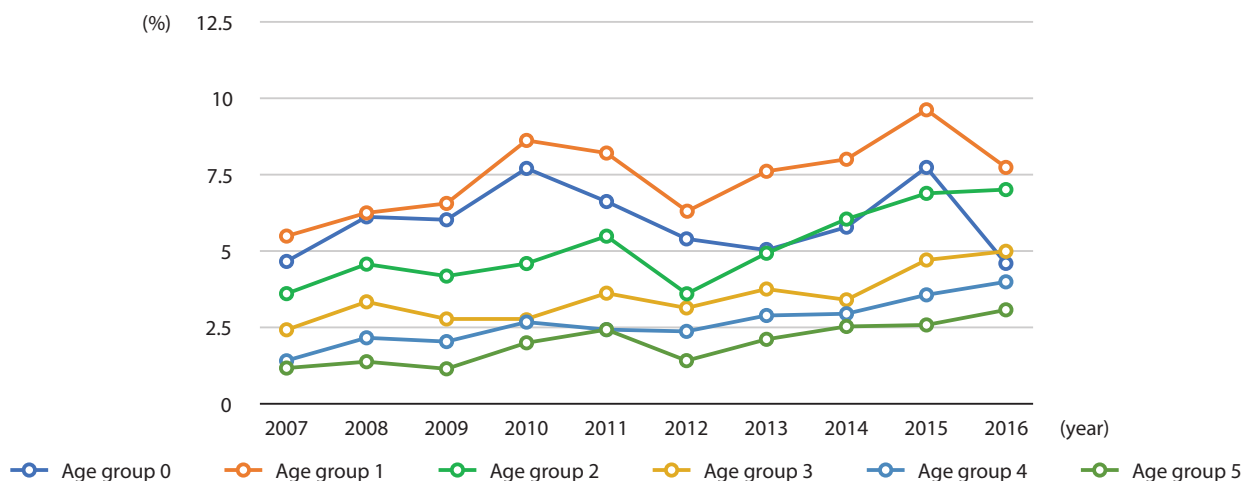


Figure 3. Comparison of food allergy prevalence among different age groups.

Age group 0; < 1 years old, Age group 1; 1- < 2 years old, Age group 2; 2- < 3 years old, Age group 3; 3- < 4 years old, Age group 4; 4- < 5 years old, Age group 5 years; 5- < 6 years old

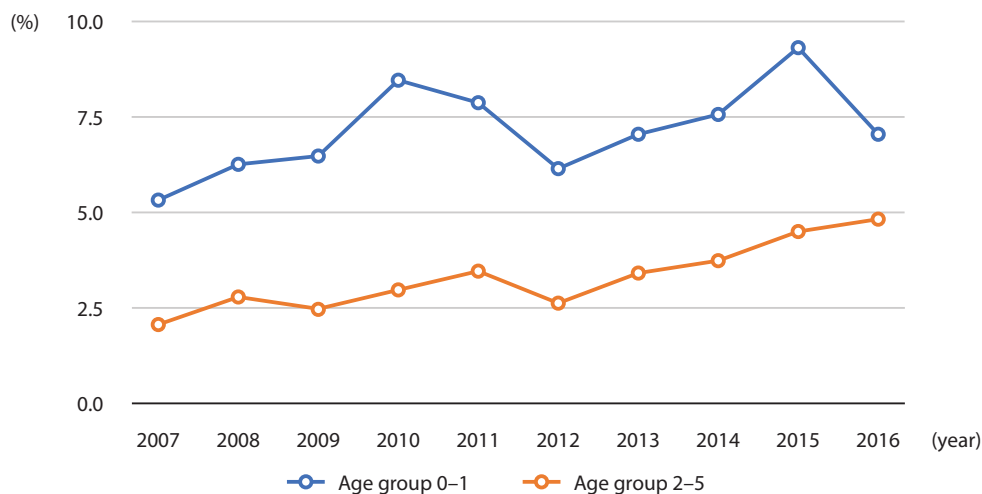


Figure 4. Comparison of food allergy prevalence between age group 0-1 and 2-5.

Age group 0-1; 0- < 2 years old, Age group 2-5; 2- < 6 years old

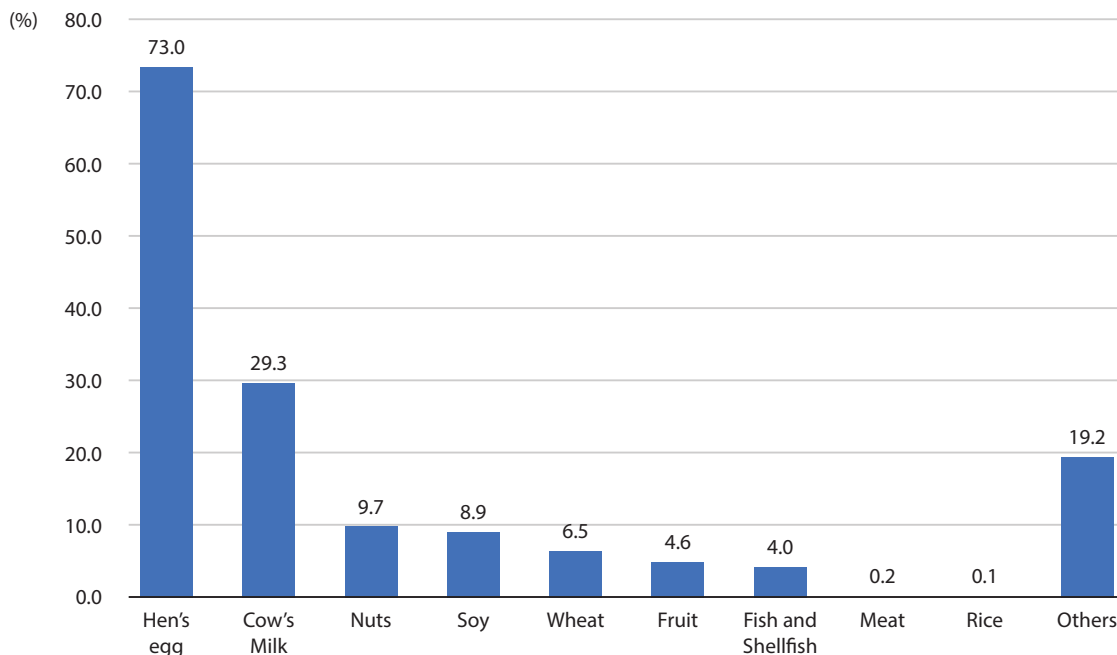


Figure 5. Causative food of food allergy in nursery children.

high prevalence of food allergy was observed among younger children, older children showed a higher increase in food allergy prevalence. We evaluated food allergy prevalence between age group 0–1 (0– < 2 years old) and age group 2–5 (2– < 6 years old) (Figure 4). It was observed that the increase of food allergy prevalence was higher in age group 2–5 than in age group 0–1 (2.0% to 4.7% vs. 5.3% to 7.0%, respectively),

whereas there were substantial fluctuations in food allergy among age group 0–1 without remarkable trend of increase.

Data from 2016 were analyzed in terms of causative foods for food avoidance. A total of 73% of the total number of food avoidance cases were caused by hen's eggs, whereas 29.3% were caused by cow's milk, 9.7% by nuts, 8.9% by soy, and 6.5% by wheat (Figure 5).

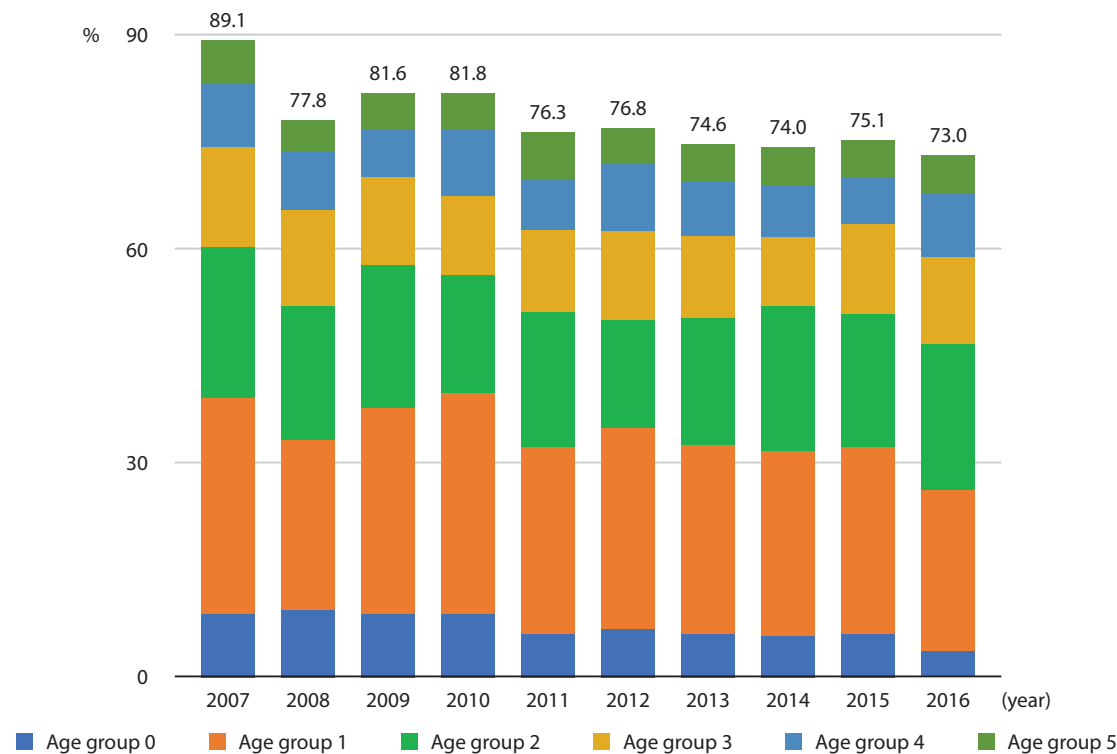
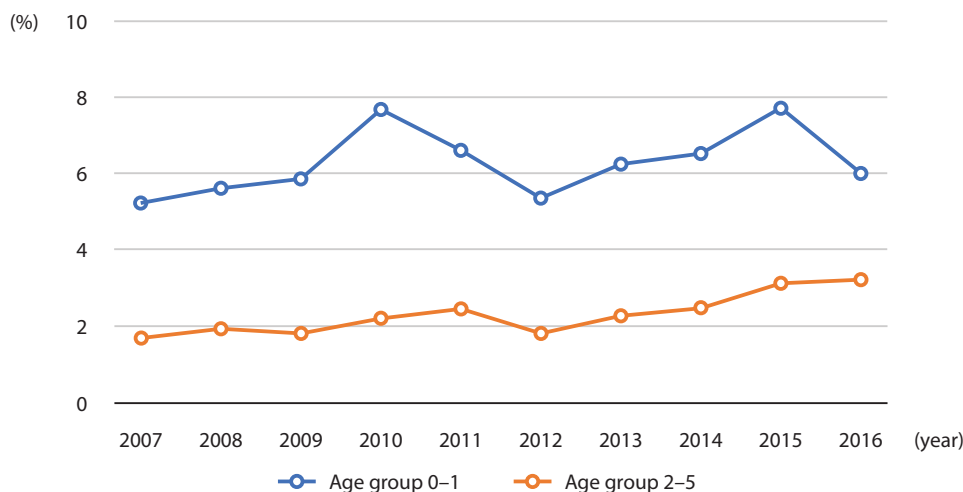


Figure 6A. Hen's egg as causative food in food allergy children.

Age group 0; < 1 years old, Age group 1; 1– < 2 years old, Age group 2; 2– < 3 years old, Age group 3; 3– < 4 years old, Age group 4; 4– < 5 years old, Age group 5; 5– < 6 years old



**Figure 6B. Comparison of egg allergy prevalence between age group 0-1 and 2-5.**

Age group 0-1; 0- < 2years old, Age group 2-5; 2- < 6years old

Hen's eggs consistently accounted for more than 70% (73.0%–89.1%) of food avoidance cases, over the analyzed 10 year period (**Figure 6A**). The prevalence of egg allergy children requiring avoidance of hen's egg as causative food in the nurseries increased significantly from 2.4% to 3.8% between 2007 and 2016 ( $P < 0.01$ ). The prevalence of egg allergy between age group 0-1 and age group 2-5 was evaluated (**Figure 6B**). It was observed that the increase of egg allergy prevalence was higher in age group 2-5 than in age group 0-1 (1.7% to 3.2% vs. 5.2% to 6.0%, respectively).

In 2016, 31 cases were instructed by primary care doctors on the emergency use of an epinephrine auto-injector in the nurseries. No reports of serious food allergy incidents or use of the epinephrine auto-injector occurred in any nursery between 2007 and 2016.

## Discussion

The prevalence of food allergies in nursery children is increasing considerably in the city of Kawasaki, Japan, currently causing a huge impact in nurseries. A more substantial increase in food allergy was observed in 2-5 year-old than in 0-1 year-old children, with no significant increase in the latter group.

Although several possible reasons for the increasing prevalence of food allergies have been put forward,<sup>3</sup> its specific causes remain unclear. Although an increasing prevalence of food allergies has been reported in children,<sup>4</sup> reliable population-based data are limited. The key reason for the lack of evidence regarding the causes for the changing prevalence of food allergies is related with methodological issues, such as selection bias in the sampling methodology and response rates, varying definitions of food allergies, and differences in the age groups and/or foods under study.<sup>3</sup>

The data from the present study were sampled in a specific region—Kawasaki city, and from a uniform study sample—nursery children. Our study therefore presents reliable data on food allergies based on medical doctors' diagnosis. These data are relevant to study the underlying causes of the increasing food allergy prevalence.

Food allergies have been reported as being most commonly acquired during the first year of life, with a peak incidence of 5%–10% at 1 year.<sup>5</sup> The prevalence falls until late childhood, reaching a plateau through adulthood.<sup>4,6</sup> The present study showed that the increasing prevalence of food allergies in older children was more substantial than in younger children. Regarding egg allergy, our study showed that the increase observed in older children was more remarkable than in younger children. The vast majority of egg allergy cases are outgrown by school-age years.<sup>5</sup> It is reported that 50% of egg allergy children develop a tolerance by the age of 4–4.5 years.<sup>7</sup>

The early intake of some foods may be beneficial as an early intervention to prevent food allergies.<sup>8,9</sup> In addition, successful food allergy desensitization has been first reported in 1908.<sup>10</sup> Recently, oral immunotherapy emerged as the most actively investigated therapeutic food allergy approach.<sup>11-14</sup> It has previously been reported that strict allergen avoidance is not always necessary for treatment. Exposure may be therapeutic, and extended delay in introduction of food allergens to the diet of young children may increase allergy risk.<sup>15</sup> Although various breakthrough diet therapies for food allergies have emerged, such as early food introduction for infants and alternative food eliminations, controversy remains regarding their efficacy and safety.<sup>16</sup> Strict food avoidance is necessary for allergy children in whom exposure to small amounts of food proteins can elicit allergic reactions. Whereas, particularly in case of egg allergy, regular ingestion of safer, less allergic forms of egg protein into the diet of egg allergy children can accelerate the development of tolerance to regular egg.<sup>17</sup> Therefore, it is possible that strict dietary avoidance of egg for egg allergy children who can ingest safe form protein or small amounts of egg may cause to hinder the development of tolerance to egg. The development delay of tolerance in egg allergy children can induce the increase of egg allergy in older children. All our study subjects have required food avoidance, therefore dietary avoidance of egg may be associated with the increase of egg allergy in older children. However, the association between the diet and the tolerance of offending foods is still unknown sufficiently.

Further studies are required to identify the causes behind the increasing prevalence of food allergies, to hen's egg in particular.

The present study has several limitations. First, although the identification of food allergy children was based on certification by their primary care doctor, no mandatory instructions regarding the food allergy diagnosis were available for nursery certification. It was, therefore, not possible to verify whether primary care doctors could definitely diagnose food allergies in every nursery child. The severity and type of food allergy, including serum IgE level in the subjects, was not clear. The Japanese Pediatric Guideline for Food Allergy 2012, published by the Japanese Society of Pediatric Allergy and Clinical Immunology in 2011,<sup>18</sup> presents standard methods to diagnose pediatric food allergies. The guideline indicates that a detailed clinical history is essential to diagnose and guide further testing, including IgE measurement or skin prick test. Besides reviewing clinical history and laboratory results, oral challenge tests should be conducted as needed.<sup>19</sup> Since the guideline integrates existing care for children with food allergies in Japan, the indicated methods for food allergy diagnosis are common to all medical doctors in Japan. Therefore, it is assumed that food allergy has been diagnosed in all children using the methods indicated in the guideline.

Second, although substantial fluctuation of food allergies was observed in 0–1 year-old children, the reason for this remains unclear. The considerable variety of food allergy symptoms requires several processes to reach a definitive diagnosis.<sup>20,21</sup> In particular, diagnosing food allergies in children constitutes a burden to some doctors. In some cases, ensuring the children's safety requires instructing them in terms of food avoidance, even in the absence of a definitive diagnosis. This fact may constitute a reason for the instability of food allergy prevalence among infants. Although our study revealed an increasing prevalence of food allergy in nursery children in Kawasaki city, further studies are needed to investigate the association between the type of food allergy including causative food, symptom severity, and serum IgE level with the epidemiology of food allergy in childhood under the strict instructions of the primary care doctors' diagnosis. In particular, the association between the prevalence of food allergy and its type should be investigated by performing observations over time.

The increase of food allergy in childhood constitutes an important health issue due to its huge impact. Food allergies, to hen's egg in particular, have increased considerably among nursery children in the city of Kawasaki, Japan, and that increase was higher among older children. Therefore, its causes must be further investigated to establish appropriate care measures that ensure the safety of children with food allergies.

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## Author contributions

- Mitsunobu Kaneko designed the study
- Mitsunobu Kaneko and Tomoko Miyoshi collected and analyzed data
- Natsuki Nakajima, Akira Shimizu, and Nobuhiro Sumida helped Mitsunobu Kaneko and Tomoko Miyoshi to collect and analyze data
- Mitsunobu Kaneko wrote the manuscript
- Yoshihiro Miyashita, Keiko Onogi, and Yuji Okano gave technical support and conceptual advice.
- All authors read and approved the final manuscript.

## Authors' affirmations

All authors of this research paper have directly participated in the planning, execution, or analysis of the study. All authors of this paper have read and approved the final version submitted.

## Conflict of interests

We declare the authors have no conflict of interests.

## Disclosure

The author has no conflict of interest to disclose with respect to this presentation.

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